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L8 ANSWER 1 OF 41 CA COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 131:82842 CA  
TITLE: Enadoline, a selective .kappa.-opioid receptor  
**agonist** shows potent antihyperalgesic and  
antiallodynic actions in a rat model of surgical pain.  
AUTHOR(S): Field, Mark John; Carnell, Anthony James; Gonzalez,  
Maria Isabel; McCleary, Scott; Oles, Ryszard Jan;  
Smith, Robert; Hughes, John; Singh, Lakhbir  
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Department  
of Biology, Cambridge University Forvie Site, Robinson  
Way, Cambridge, CB2 2QB, UK  
SOURCE: Pain (1999), 80(1,2), 383-389  
CODEN: PAINDB; ISSN: 0304-3959  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d kwic

L8 ANSWER 1 OF 41 CA COPYRIGHT 2002 ACS  
TI Enadoline, a selective .kappa.-opioid receptor **agonist** shows  
potent antihyperalgesic and antiallodynic actions in a rat model of  
surgical pain.  
AB Enadoline is a highly selective and potent .kappa.-opioid receptor  
**agonist**. This report describes and compares the activities of  
enadoline and morphine in a rat model of postoperative pain. A 1. . .  
that administration of morphine (1-6 mg/kg, s.c.) 0.5 h before surgery can  
prevent the development of thermal hyperalgesia with a **MED** of  
.ltoreq.1 mg/kg, but has little effect on static allodynia. In the  
present study similar administration of morphine (1-3 mg/kg),. . .  
IT Pain  
Skin, disease  
(allodynia; enadoline, a selective .kappa.-opioid receptor  
**agonist** shows potent antihyperalgesic and antiallodynic actions  
in a rat model of surgical pain.)  
IT Analgesics  
(enadoline, a selective .kappa.-opioid receptor **agonist** shows  
potent antihyperalgesic and antiallodynic actions in a rat model of  
surgical pain.)  
IT Breathing (animal)  
(isoflurane-induced respiratory depression; enadoline, a selective  
.kappa.-opioid receptor **agonist** shows potent antihyperalgesic  
and antiallodynic actions in a rat model of surgical pain.)  
IT Opioids  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(.kappa.-; enadoline, a selective .kappa.-opioid receptor  
**agonist** shows potent antihyperalgesic and antiallodynic actions  
in a rat model of surgical pain.)

IT 57-27-2, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (comparison; enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)

IT 124378-77-4, Enadoline  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (enadoline, a selective .kappa.-opioid receptor **agonist** shows potent antihyperalgesic and antiallodynic actions in a rat model of surgical pain.)

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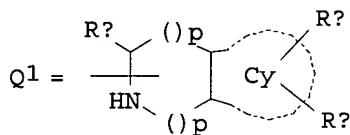
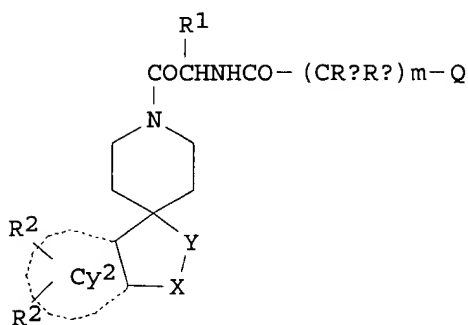
L13 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 132:22957 CA  
 TITLE: Preparation of spiroperidine derivatives as **melanocortin** receptor agonists  
 INVENTOR(S): Nargund, Ravi P.; Ye, Zhixiong; Palucki, Brenda L.; Bakshi, Raman K.; Patchett, Arthur A.; Van Der Ploeg, Leonardus H. T.  
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA  
 SOURCE: PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964002	A1	19991216	WO 1999-US13252	19990610
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946801	A1	19991230	AU 1999-46801	19990610
AU 742425	B2	20020103		
EP 1085869	A1	20010328	EP 1999-930220	19990610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
US 6294534	B1	20010925	US 1999-329814	19990610
JP 2002517444	T2	20020618	JP 2000-553071	19990610
US 2001029259	A1	20011011	US 2001-781373	20010212
US 6410548	B2	20020625		
PRIORITY APPLN. INFO.:			US 1998-88908P	P 19980611
			GB 1998-17179	A 19980806
			US 1999-123260P	P 19990308
			US 1999-329814	A3 19990610
			WO 1999-US13252	W 19990610
OTHER SOURCE(S):			MARPAT 132:22957	
REFERENCE COUNT:			3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT	

09/990,499

=> d 113 16 abs

L13 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS  
GI



AB Certain novel spiropiperidine compds. I [Cy2 = six-membered arom. ring contg. 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclcyl, 5 or 6 membered carbocyclcyl; m, p, q independently = 0, 1, or 2] are agonists of **melanocortin** receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of **melanocortin** receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

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=> d ibib abs kwic 1-16

L20 ANSWER 1 OF 16 CA COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 137:52344 CA  
TITLE: Treatment of male **sexual dysfunction**  
INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn;  
Wayman, Christopher Peter  
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.  
SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047670	A1	20020620	WO 2001-IB2399	20011210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002028799	A1	20020307	US 2001-895367	20010629
US 2002102707	A1	20020801	US 2001-905846	20010713
PRIORITY APPLN. INFO.:			GB 2000-30647	A 20001215
			GB 2001-8730	A 20010406
			GB 2001-9910	A 20010423
			GB 2001-11037	A 20010504
			US 2001-895367	A 20010629
			US 2001-905846	A 20010713
			GB 2001-20679	A 20010824
			GB 2000-16684	A 20000706
			GB 2000-17387	A 20000714
			US 2000-219100P	P 20000718
			US 2000-220908P	P 20000726
			US 2001-265358P	P 20010131
			GB 2001-6167	A 20010313
			GB 2001-8483	A 20010404
AB	The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor assocd. with male genitalia, in the prepn./manuf. of a medicament for the treatment or prevention of <b>male erectile dysfunction</b> (MED).			
REFERENCE COUNT:	7	THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		
TI	Treatment of male <b>sexual dysfunction</b>			
AB	The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor assocd. with male genitalia, in the prepn./manuf. of a medicament for the treatment or prevention of <b>male erectile dysfunction</b> (MED).			
ST	male <b>sexual dysfunction</b> neuropeptide Y inhibitor sequence			
IT	5-HT receptors			
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (5-HT1A, modulators; neuropeptide Y inhibitors for treatment of male <b>sexual dysfunction</b> )			
IT	5-HT receptors			
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (5-HT2A, modulators; neuropeptide Y inhibitors for treatment of male <b>sexual dysfunction</b> )			
IT	5-HT receptors			
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (5-HT3, modulators; neuropeptide Y inhibitors for treatment of male			

**sexual dysfunction)**

IT 5-HT receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (5HT6, modulators; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Dopamine agonists  
 (D2; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Dopamine agonists  
 (D3; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Opioid receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (ORL1, agonists; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Neuropeptide Y receptors  
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (Y1; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Estrogens  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (agonists; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Bombesin receptors  
 Endothelin receptors  
 Gastrin-releasing peptide receptors  
 Tachykinin receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Estrogens  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antiestrogens; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Appetite  
 (bulimia; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Ion channel blockers  
 (calcium; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Drug delivery systems  
 (carriers; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Penis  
 (corpus cavernosum; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Appetite  
 (disorder; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Alkaloids, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ergot; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Prostaglandins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (esters; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Sexual behavior  
 (impotence; neuropeptide Y inhibitors for treatment of male

**sexual dysfunction)**

IT Potassium channel  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (intermediate conductance calcium-activated, modulators; neuropeptide Y  
 inhibitors for treatment of male **sexual dysfunction**  
 )

IT Reproductive organ  
 (male; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Pituitary hormone receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (**melanocortin**, agonists; neuropeptide Y inhibitors for  
 treatment of male **sexual dysfunction)**

IT Transport proteins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (modulators of, for noradrenaline, dopamine, and serotonin;  
 neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Cannabinoid receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (modulators; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT 5-HT agonists  
 5-HT antagonists  
 Anesthesia  
 Anorexia  
 Anticholesteremic agents  
 Anticoagulants  
 Antidiabetic agents  
 Antiobesity agents  
 Blood pressure  
 Dopamine agonists  
 Fluorometry  
 Human  
 Nervous system agents  
 Obesity  
 Opioid antagonists  
 Platelet aggregation inhibitors  
 Protein sequences  
 Purinoceptor agonists  
 Vasodilators  
 cDNA sequences  
 (neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Estrogens  
 Opioids  
 Prostaglandins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Anti-inflammatory agents  
 (nonsteroidal; neuropeptide Y inhibitors for treatment of male  
**sexual dysfunction)**

IT Drug delivery systems  
 (oral; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Nerve  
 (pelvic; neuropeptide Y inhibitors for treatment of male **sexual  
 dysfunction)**

IT Sexual behavior

- (penile erection; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT Ion channel openers  
(potassium; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT Anti-inflammatory agents  
(steroidal; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT Bombesin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(type BB1, antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT Bombesin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(type BB2, antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT Bombesin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(type BB3, antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT Adrenoceptor antagonists  
(.alpha.-; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 72162-96-0, Thromboplastin  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(-activating factor inhibitors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(-sensitizing agents; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 9036-21-9  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(III, inhibitors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 50-56-6, Oxytocin, biological studies 57576-52-0, Thromboxane a2  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(agonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 138238-81-0, Endothelin converting enzyme  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antagonists; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 10102-43-9, Nitric oxide, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(donors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 9028-35-7  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitors, statins; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 9000-81-1, Acetylcholinesterase 9002-04-4, Thrombin 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase v 9068-54-6, Phosphodiesterase ii 82785-45-3, Neuropeptide Y  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; neuropeptide Y inhibitors for treatment of male **sexual dysfunction**)
- IT 9015-82-1, Angiotensin converting enzyme  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(neuropeptide Y inhibitors for treatment of male **sexual**

**dysfunction)**

IT 58-00-4, Apomorphine 58-18-4, Methyl testosterone 58-22-0, Tostrelle 59-92-7, L Dopa, biological studies 63-05-8D, Androstenedione, derivs. 74-79-3, L Arginine, biological studies 81-81-2, Warfarin 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 8001-27-2, Hirudin 9005-49-6, Heparin, biological studies 9039-53-6, Urokinase plasminogen activator 28860-95-9, Carbidopa 29094-61-9, Glipizide 37221-79-7, Vasoactive intestinal peptide 82707-54-8, Neutral endopeptidase 85637-73-6, Atrial natriuretic factor 88150-42-9, Amlodipine 97322-87-7, Rezulin 114471-18-0, Atrial natriuretic peptide b 114798-26-4, Losartan 120014-06-4, Donepezil 127830-04-0, Atrial natriuretic peptide c 128908-32-7, **Melanocortin** 134523-00-5, Atorvastatin 139639-23-9, Tissue plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuropeptide Y inhibitors for treatment of male **sexual**

**dysfunction)**

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(transporters for; neuropeptide Y inhibitors for treatment of male

**sexual dysfunction)**

IT 438443-44-8 438443-45-9 438443-46-0 438443-47-1 438443-48-2

RL: PRP (Properties)

(unclaimed nucleotide sequence; treatment of male **sexual**

**dysfunction)**

IT 438443-49-3

RL: PRP (Properties)

(unclaimed protein sequence; treatment of male **sexual**

**dysfunction)**

IT 438190-17-1

RL: PRP (Properties)

(unclaimed sequence; treatment of male **sexual**

**dysfunction)**

L20 ANSWER 2 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:395983 CA

TITLE: Bombesin receptor antagonists, and combinations with other agents, for the treatment of **sexual dysfunction**

INVENTOR(S): Gonzalez, Maria Isabel; Stock, Herman Thijs; Pinnock, Robert Denham; Pritchard, Martyn Clive; Wayman, Christopher Peter; Van der Graaf, Pieter Hadewijn; Naylor, Alisdair Mark; Higginbottom, Michael

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 225 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040008	A2	20020523	WO 2001-GB5018	20011114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				



RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002040022 A1 20020523 WO 2000-GB4380 20001117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2000-GB4380 W 20001117  
GB 2001-9910 A 20010423  
GB 2001-11037 A 20010504

OTHER SOURCE(S): MARPAT 136:395983

AB Bombesin receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of bombesin receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Prepn. of compds. of the invention is described.

TI Bombesin receptor antagonists, and combinations with other agents, for the treatment of **sexual dysfunction**

AB Bombesin receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of bombesin receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Prepn. of compds. of the invention is described.

ST bombesin receptor antagonist **sexual dysfunction** treatment; phosphodiesterase inhibitor bombesin antagonist **sexual dysfunction** treatment; neutral endopeptidase inhibitor bombesin antagonist prepn **sexual dysfunction** treatment; lasofoxifene bombesin antagonist **sexual dysfunction** treatment

IT Nervous system agents  
(CNS-active; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Oxytocin receptors  
Vasopressin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(agonists and modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT VIP receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(agonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Estrogens  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(and agonists and antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT Prostaglandins  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

- (Biological study); USES (Uses)  
(and prostaglandin esters; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Gastrin-releasing peptide receptors  
Tachykinin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Steroids, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(antiinflammatory; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Behavior  
(arousal, sexual arousal disorders; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 5-HT agonists  
5-HT antagonists  
Angiotensin receptor antagonists  
Anti-inflammatory agents  
Anticholesteremic agents  
Anticoagulants  
Antidiabetic agents  
Dopamine agonists  
Drug delivery systems  
Drug interactions  
Hormone replacement therapy  
Human  
Opioid antagonists  
Platelet aggregation inhibitors  
Purinoceptor agonists  
Vasodilators  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Bombesin receptors  
Sex hormones  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Opioids  
Peptides, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Ion channel blockers  
(calcium; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Resolution (separation)  
(chromatog.; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Sexual behavior  
(disorder; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Transport proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(dopamine-transporting, modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual**

- dysfunction)**
- IT Drugs
  - (drug-induced **sexual dysfunction**; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Alkaloids, biological studies
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (ergot; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Drug delivery systems
  - (implants, testosterone; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Sexual behavior
  - (impotence; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Pituitary hormone receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (**melanocortin**, agonists and modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 5-HT receptors
  - Cannabinoid receptors
  - Estrogen receptors
  - Opioid receptors
  - Potassium channel
  - Purinoceptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Anti-inflammatory agents
  - (nonsteroidal; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Transport proteins
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (norepinephrine-transporting, modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Drug delivery systems
  - (oral; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Ion channel openers
  - (potassium; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Transport proteins
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (serotonin-transporting, modulators; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Antidepressants
  - (**sexual dysfunction** induced by; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Analgesics
  - (sexual pain disorders; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Bombesin receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (type BB1, antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Bombesin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(type BB2, antagonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT Adrenoceptor antagonists  
(.alpha.-; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 57576-52-0, Thromboxane A2  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(agonists; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 58-22-0, Testosterone  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(and replacement agents; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 50-28-2, Estradiol, biological studies 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 57-83-0, Progesterone, biological studies  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P 425638-96-6P  
425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P 425639-07-2P  
425639-10-7P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P  
425639-25-4P 425639-28-7P 425639-31-2P 425639-33-4P 425639-35-6P  
425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P 425639-45-8P  
425639-47-0P 425639-48-1P 425639-49-2P 425639-50-5P 425639-53-8P  
425639-55-0P 425639-57-2P 425639-59-4P 425639-61-8P 425639-65-2P  
425639-68-5P 425639-70-9P 425639-72-1P 425639-74-3P 425639-76-5P  
425639-77-6P 425639-79-8P 425639-81-2P 425639-83-4P 425639-85-6P  
425639-87-8P 425639-89-0P 425639-91-4P 425639-93-6P 425639-95-8P  
425639-96-9P 425639-97-0P 425639-98-1P 425639-99-2P 425640-00-2P  
425640-01-3P 425640-02-4P 425640-03-5P 425640-15-9P 425640-23-9P  
425641-28-7P 429657-44-3P  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 50-50-0, Estradiol benzoate 102577-19-5, Neuromedin B  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)
- IT 426213-31-2P 426213-32-3P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 58-18-4, Methyl testosterone 59-92-7, biological studies 71-58-9, Medroxyprogesterone acetate 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 28860-95-9, Carbidopa 37221-79-7, Vasoactive intestinal polypeptide 37221-79-7D, Vasoactive intestinal polypeptide, analogs 114798-26-4, Losartan 204066-72-8 204066-73-9 204066-75-1 204066-76-2 204066-78-4 204066-79-5 204066-80-8 204066-82-0 204066-83-1 204066-84-2 204066-86-4 204066-87-5 204066-89-7 204066-93-3 204066-95-5 204067-01-6 204067-38-9 215297-27-1 425640-04-6 425640-06-8 425640-08-0 425640-09-1 425640-10-4 425640-11-5 425640-12-6 425640-14-8 425640-17-1 425640-18-2 425640-20-6 425640-21-7 425640-24-0 425640-26-2 425640-28-4 425640-30-8 425640-32-0 425640-34-2 425640-36-4 425640-38-6 425640-39-7 425640-40-0 425640-41-1 425640-43-3 425640-45-5 425640-47-7 425640-49-9 425640-51-3 425640-53-5 425640-55-7 425640-57-9 425640-59-1 425640-60-4 425640-62-6 425640-66-0 425640-68-2 425640-70-6 425640-72-8 425640-74-0 425640-76-2 425640-78-4 425640-80-8 425640-82-0 425640-83-1 425640-84-2 425640-85-3 425640-86-4 425640-87-5 425640-88-6 425640-89-7 425640-90-0 425640-91-1 425640-92-2 425640-93-3 425640-94-4 425640-95-5 425640-96-6 425640-97-7 425640-98-8 425640-99-9 425641-00-5 425641-01-6 425641-02-7 425641-03-8 425641-04-9 425641-05-0 425641-06-1 425641-07-2 425641-08-3 425641-09-4 425641-10-7 425641-11-8 425641-12-9 425641-13-0 425641-14-1 425641-15-2 425641-16-3 425641-17-4 425641-18-5 425641-19-6 425641-20-9 425641-21-0 425641-22-1 425641-23-2 425641-24-3 425641-25-4 425641-26-5 425641-27-6 425641-29-8 425641-30-1 428864-38-4 428864-39-5 428864-40-8 428864-41-9 428864-42-0 428864-43-1 428864-44-2 428864-45-3 428864-46-4 428864-47-5 428864-48-6 428864-49-7 428864-50-0 428864-51-1 428864-52-2 428864-53-3 428864-54-4 428864-55-5 428864-56-6 428864-57-7 428864-58-8 428864-59-9 428864-63-5 428864-64-6 428864-66-8 428864-67-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 388630-36-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 337962-74-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 10102-43-9, Nitric oxide, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(donors; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 128908-32-7, **Melanocortin**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(enhancers; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 9000-81-1, Acetylcholinesterase 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase V 82707-54-8, Neutral endopeptidase 82785-45-3, Neuropeptide Y  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; bombesin receptor antagonists, and combinations with other agents, for treatment of **sexual dysfunction**)

IT 9088-07-7, Natriuretic factor

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(modulators; bombesin receptor antagonists, and combinations with other  
agents, for treatment of **sexual dysfunction**)

IT 25506-37-0P 31558-54-0P 63430-65-9P 73717-05-2P 97534-88-8P  
97557-59-0P 105754-24-3P 137140-98-8P 158556-65-1P 158951-86-1P  
159672-85-2P 159672-86-3P 160233-08-9P 172154-13-1P 172154-15-3P  
172154-17-5P 172154-18-6P 204067-15-2P 204067-16-3P 204067-17-4P  
291761-10-9P 337962-91-1P 388630-99-7P 425641-31-2P 425641-32-3P  
425641-33-4P 425641-34-5P 425641-39-0P 425641-46-9P 425641-47-0P  
425641-48-1P 425641-49-2P 425641-50-5P 425641-51-6P 425641-52-7P  
425641-53-8P 428864-72-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(prepn. and reaction; bombesin receptor antagonists, and combinations  
with other agents, for treatment of **sexual  
dysfunction**)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid  
65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid  
85-46-1, 1-Naphthalenesulfonyl chloride 86-59-9, Quinoline-8-carboxylic  
acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic  
acid 89-95-2 93-03-8 93-11-8, 2-Naphthalenesulfonyl chloride  
93-25-4, (2-Methoxyphenyl)acetic acid 98-31-7 98-59-9 98-60-2  
98-74-8 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic  
acid 99-64-9, 3-Dimethylaminobenzoic acid 99-81-0 99-94-5,  
4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8,  
(4-Methoxyphenyl)acetic acid 104-03-0, (4-Nitrophenyl)acetic acid  
105-13-5 108-86-1, Bromobenzene, reactions 118-90-1, 2-Methylbenzoic  
acid 118-91-2, 2-Chlorobenzoic acid 121-51-7 122-78-1,  
Benzeneacetaldehyde 156-38-7, (4-Hydroxyphenyl)acetic acid 349-75-7  
349-88-2 349-95-1 445-29-4, 2-Fluorobenzoic acid 446-51-5  
451-82-1, (2-Fluorophenyl)acetic acid 488-93-7, Furan-3-carboxylic acid  
527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid  
552-16-9, 2-Nitrobenzoic acid 555-16-8, 4-Nitrobenzaldehyde, reactions  
579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid  
587-03-1 589-18-4 591-17-3, 1-Bromo-3-methylbenzene 605-65-2  
610-16-2, 2-Dimethylaminobenzoic acid 612-16-8 613-89-8 615-18-9,  
2-Chlorobenzoxazole 619-25-0 619-73-8 621-36-3, m-Tolylacetic acid  
621-37-4, (3-Hydroxyphenyl)acetic acid 622-47-9, p-Tolylacetic acid  
644-36-0, o-Tolylacetic acid 673-06-3, D-Phenylalanine 701-27-9  
776-04-5 777-44-6 873-76-7 874-97-5 877-65-6 879-65-2,  
Quinoxaline-2-carboxylic acid 931-97-5, 1-Hydroxycyclohexanecarbonitrile  
934-60-1, 6-Methylpyridine-2-carboxylic acid 1477-50-5,  
1H-Indole-2-carboxylic acid 1592-38-7, 2-Naphthalenemethanol 1656-44-6  
1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic  
acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8 1805-32-9  
1877-72-1, 3-Cyanobenzoic acid 1899-93-0 1918-79-2,  
5-Methylthiophene-2-carboxylic acid 1939-99-7, Benzenemethanesulfonyl  
chloride 2104-06-5 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6,  
[1,1'-Biphenyl]-2-sulfonyl chloride 2766-74-7 2888-06-4 2905-21-7  
2905-23-9 2991-42-6 3405-77-4, 5-Methylisoxazole-3-carboxylic acid  
3622-35-3, Benzothiazole-6-carboxylic acid 4052-30-6,  
4-Methanesulfonylbenzoic acid 4254-29-9 4265-16-1,  
Benzofuran-2-carbaldehyde 4533-95-3 4533-96-4 4780-79-4,  
1-Naphthalenemethanol 5345-27-7 6314-28-9, Benzo[b]thiophene-2-  
carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2,  
3-Thiopheneacetic acid 6973-60-0 7693-46-1, p-Nitrophenyl  
chloroformate 10130-74-2 10333-68-3, 2-Pyrrol-1-ylbenzoic acid  
13826-35-2 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole 15084-51-2  
16136-58-6, 1-Methyl-1H-indole-2-carboxylic acid 16629-19-9,  
2-Thiophenesulfonyl chloride 16709-25-4 17078-28-3,

(4-Dimethylaminophenyl)acetic acid 17849-38-6 18704-37-5,  
 8-Quinolinesulfonyl chloride 23095-31-0 23806-24-8,  
 3-Methylthiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-  
 carboxylic acid 24424-99-5, Di-tert-butyl dicarbonate 24974-75-2  
 26638-43-7 28286-86-4 38594-42-2 39774-26-0, 2-Bromo-6-  
 phenylpyridine 42413-03-6 49584-26-1 51527-73-2 54997-92-1  
 56542-67-7 56946-83-9 59337-92-7 69360-26-5 71648-21-0  
 73713-79-8 80466-79-1 82964-91-8 88398-93-0 91170-93-3  
 94108-56-2 99924-18-2 100516-88-9, 6-Quinolinemethanol 114322-14-4,  
 2,1,3-Benzoxadiazole-4-sulfonyl chloride 118783-85-0 137049-00-4  
 137049-02-6 142854-50-0 151858-64-9 160233-27-2 166964-37-0  
 185908-35-4 204067-08-3 204067-12-9 206262-15-9 206262-83-1  
 216394-05-7 216394-11-5 425641-35-6 425641-36-7 425641-37-8  
 425641-38-9 425641-40-3 425641-41-4 425641-42-5 425641-43-6  
 425641-45-8 426213-33-4 426213-34-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; bombesin receptor antagonists, and combinations with other  
 agents, for treatment of **sexual dysfunction**)

IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (sensitizing agents; bombesin receptor antagonists, and combinations  
 with other agents, for treatment of **sexual dysfunction**)

IT 125978-95-2, Nitric oxide synthase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (substrates; bombesin receptor antagonists, and combinations with other  
 agents, for treatment of **sexual dysfunction**)

L20 ANSWER 3 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:216648 CA

TITLE: Preparation of substituted piperidines as  
**melanocortin** receptor agonists

INVENTOR(S): Bakshi, Raman K.; Barakat, Khaled J.; Lai, Yingjie;  
 Nargund, Ravi P.; Palucki, Brenda L.; Park, Min K.;  
 Patchett, Arthur A.; Sebhat, Iyassu; Ye, Zhixiong

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 128 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

AU 2001088285 A5 20020304 AU 2001-88285 20010817

PRIORITY APPLN. INFO.: US 2000-227180P P 20000823

WO 2001-US25757 W 20010817

OTHER SOURCE(S): MARPAT 136:216648

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\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; X = C1-8 alkyl, alkylencycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; X = C1-8 alkyl, alkylencycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; R1 = H, C1-8 alkyl, alkylencycloalkyl, alkylenearyl, alkyleneheteroaryl; Q = amino-tetrahydronaphthyl, amino-benzocycloheptyl, methylamino-tetrahydronaphthyl, aminoindanyl, amino-benzothiopyranyl, amino-1,4-dihydro-1,4-methanonaphthyl, etc.; n = 0, 1, 2], stereoisomers, and pharmaceutically acceptable salts are prepd. as agonists of the human **melanocortin** receptors and, in particular, as selective agonists of the human **melanocortin-4** receptor (MC-4R). Title compds. I are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Pharmaceutical compn. including title compds. I and second active ingredient are claimed. Thus, the title compd. II was prepd. from 4-F-D-Phe-4-cyclohexyl-piperidine-4-carboxylic acid Et ester HCl salt and cis-1,2,3,4-tetrahydro-1-tert-butoxycarbonyl-naphthalene-2-carboxylic acid, which was prepd. from 1,2-dihydroaphthalene, ClSO<sub>2</sub>NCO.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of substituted piperidines as **melanocortin** receptor agonists

AB Title compds. [I; X = C1-8 alkyl, alkylencycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; X = C1-8 alkyl, alkylencycloalkyl, alkylenearyl, alkyleneheteroaryl, etc.; R1 = H, C1-8 alkyl, alkylencycloalkyl, alkylenearyl, alkyleneheteroaryl; Q = amino-tetrahydronaphthyl, amino-benzocycloheptyl, methylamino-tetrahydronaphthyl, aminoindanyl, amino-benzothiopyranyl, amino-1,4-dihydro-1,4-methanonaphthyl, etc.; n = 0, 1, 2], stereoisomers, and pharmaceutically acceptable salts are prepd. as agonists of the human **melanocortin** receptors and, in particular, as selective agonists of the human **melanocortin-4** receptor (MC-4R). Title compds. I are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Pharmaceutical compn. including title compds. I and second active ingredient are claimed. Thus, the title compd. II was prepd. from 4-F-D-Phe-4-cyclohexyl-piperidine-4-carboxylic acid Et ester HCl salt and cis-1,2,3,4-tetrahydro-1-tert-butoxycarbonyl-naphthalene-2-carboxylic acid, which was prepd. from 1,2-dihydroaphthalene, ClSO<sub>2</sub>NCO.

ST piperidine prepn **melanocortin** receptor agonist

IT Sexual behavior  
(disorder; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Sexual behavior  
(impotence; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Pituitary hormone receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**melanocortin 4**; prepn. of substituted piperidines as **melanocortin** receptor agonists)

IT Pituitary hormone receptors



RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (melanocortin; prepn. of substituted piperidines as  
 melanocortin receptor agonists)

IT Diabetes mellitus  
 Human  
 Obesity

(prepn. of substituted piperidines as melanocortin receptor  
 agonists)

IT	401842-86-2P	401842-90-8P	401842-92-0P	401842-94-2P	401842-95-3P
	401842-96-4P	401842-98-6P	401842-99-7P	401843-01-4P	401843-02-5P
	401843-03-6P	401843-04-7P	401843-05-8P	401843-06-9P	401843-07-0P
	401843-08-1P	401843-09-2P	401843-10-5P	401843-11-6P	401843-12-7P
	401843-13-8P	401843-14-9P	401843-15-0P	401843-16-1P	401843-17-2P
	401843-18-3P	401843-19-4P	401843-20-7P	401843-21-8P	401843-22-9P
	401843-23-0P	401843-24-1P	401843-25-2P	401843-26-3P	401843-28-5P
	401843-29-6P	401843-31-0P	401843-32-1P	401843-33-2P	401843-34-3P
	401843-35-4P	401843-36-5P	401843-37-6P	401843-38-7P	401843-39-8P
	401843-40-1P	401843-41-2P	401843-44-5P	401843-58-1P	401843-59-2P
	401843-60-5P	401843-61-6P	401843-62-7P	401843-63-8P	401843-64-9P
	401843-65-0P	401843-66-1P	401843-67-2P	401843-68-3P	401843-69-4P
	401843-94-5P	401915-20-6P	401915-23-9P	401915-27-3P	401915-31-9P
	401915-33-1P	401915-36-4P	401915-38-6P	401915-41-1P	401915-42-2P
	401915-43-3P	401915-44-4P	401915-46-6P	401915-47-7P	401915-48-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(prepn. of substituted piperidines as melanocortin receptor  
 agonists)

IT 124-68-5 447-53-0 826-73-3, 1-Benzosuberone 1189-71-5,  
 Chlorosulfonyl isocyanate 2749-11-3, (S)-(+)-2-Amino-1-propanol  
 4453-90-1, 1,4-Dihydro-1,4-methanonaphthalene 10316-79-7,  
 1-Aminocyclopentanemethanol 22059-21-8, 1-Aminocyclopropane-1-carboxylic  
 acid 29059-07-2, Tetralone 57292-44-1 57292-45-2 312638-87-2  
 401843-95-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of substituted piperidines as melanocortin receptor  
 agonists)

IT	95-13-6P, Indene	4373-13-1P	7125-62-4P	14944-28-6P	35550-94-8P
	40073-45-8P	59433-90-8P	132565-21-0P	363192-22-7P	363192-23-8P
	363192-24-9P	363192-25-0P	363192-26-1P	363192-27-2P	363192-28-3P
	363192-29-4P	363192-30-7P	363192-31-8P	363192-32-9P	363192-33-0P
	363192-34-1P	363192-35-2P	378741-77-6P	378741-78-7P	401843-45-6P
	401843-46-7P	401843-47-8P	401843-48-9P	401843-49-0P	401843-50-3P
	401843-51-4P	401843-52-5P	401843-53-6P	401843-55-8P	401843-56-9P
	401843-57-0P	401843-70-7P	401843-73-0P	401843-74-1P	401843-75-2P
	401843-76-3P	401843-77-4P	401843-78-5P	401843-79-6P	401843-80-9P
	401843-81-0P	401843-82-1P	401843-88-7P	401843-90-1P	401843-91-2P
	401843-92-3P	401843-93-4P	401843-96-7P	401843-97-8P	401843-98-9P
	401843-99-0P	401915-50-2P			

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(prepn. of substituted piperidines as melanocortin receptor  
 agonists)

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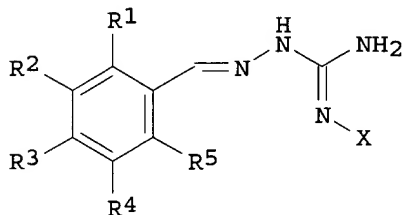
ACCESSION NUMBER: 136:167180 CA

TITLE: Preparation of N-(benzylideneamino)guanidines and  
 N-(benzylideneamino)-N'-hydroxyguanidines and their  
 use as melanocortin receptor ligands

INVENTOR(S): Lundstedt, Torbjorn; Skottner, Anna; Seifert,

Elisabeth  
 PATENT ASSIGNEE(S): Melacure Therapeutics AB, Swed.  
 SOURCE: PCT Int. Appl., 42 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011715	A2	20020214	WO 2001-GB3534	20010807
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001076522	A5	20020218	AU 2001-76522	20010807
PRIORITY APPLN. INFO.:			GB 2000-19357	A 20000807
			WO 2001-GB3534	W 20010807
OTHER SOURCE(S):			MARPAT 136:167180	
GI				



I

AB The present invention relates to the use of compds. of general formula (I; wherein X is H or OH; R1 - R5 are the same or different and are selected from hydrogen, halogen, alkyl having 1 to 5 carbon atoms, electron donor groups such as alkoxy having 1-5 carbon atoms or hydroxy, electron acceptor groups (selected from cyano, nitro, trifluoroalkyl or amide), alkylamino, benzoyloxy, nitroxy, Ph or sulfo) and the pharmacol. active salts thereof as ligands to the **melanocortin** receptors and/or for treatment of disorders in the **melanocortin** system. The above disorders related to the **melanocortin** system are inflammation, mental disorders, sexual functions and/**sexual dysfunctions**, drug-induced or other disorders of the blood and/or lymphoid system, allergic disorders, disorders of cardiovascular system, pain, diabetes type II, obesity, anorexic conditions (those caused by cancer, cachexia, geriatric conditions, HIV, trauma, and psychol. conditions), peripheral nerve regeneration, central nerve regeneration, skin disorders including melanoma, or ischemia and/or ischemia/reperfusion. These compds. are also useful for the treatment of dysfunctions of the endocrine system or an hormonal system, inducing skin tanning or for inducing lighter skin color, and for the treatment and/or diagnosis of malignancies such as melanoma and metastasis. A soln. of

2-chloro-3,4-dimethoxybenzaldehyde (1.0 g, 5 mmol), aminoguanidine bicarbonate (0.68 g, 5 mmol) and acetic acid (1 mL) in 15 mL of methanol was heated at reflux for 10 min to give 70% N-(2-chloro-3,4-dimethoxybenzylideneamino)guanidine acetate. N-(5-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate in vitro showed the binding affinity to MC1, MC3, MC4, and MC5 receptor with  $K_i$  of 6.4, 1, 17.1, and 8.7  $\mu\text{M}$ , resp.

TI Preparation of N-(benzylideneamino)guanidines and N-(benzylideneamino)-N'-hydroxyguanidines and their use as **melanocortin** receptor ligands

AB The present invention relates to the use of compds. of general formula (I; wherein X is H or OH; R1 - R5 are the same or different and are selected from hydrogen, halogen, alkyl having 1 to 5 carbon atoms, electron donor groups such as alkoxy having 1-5 carbon atoms or hydroxy, electron acceptor groups (selected from cyano, nitro, trifluoroalkyl or amide), alkylamino, benzyloxy, nitroxy, Ph or sulfo) and the pharmacol. active salts thereof as ligands to the **melanocortin** receptors and/or for treatment of disorders in the **melanocortin** system. The above disorders related to the **melanocortin** system are inflammation, mental disorders, sexual functions and/**sexual dysfunctions**, drug-induced or other disorders of the blood and/or lymphoid system, allergic disorders, disorders of cardiovascular system, pain, diabetes type II, obesity, anorexic conditions (those caused by cancer, cachexia, geriatric conditions, HIV, trauma, and psychol. conditions), peripheral nerve regeneration, central nerve regeneration, skin disorders including melanoma, or ischemia and/or ischemia/reperfusion. These compds. are also useful for the treatment of dysfunctions of the endocrine system or an hormonal system, inducing skin tanning or for inducing lighter skin color, and for the treatment and/or diagnosis of malignancies such as melanoma and metastasis. A soln. of 2-chloro-3,4-dimethoxybenzaldehyde (1.0 g, 5 mmol), aminoguanidine bicarbonate (0.68 g, 5 mmol) and acetic acid (1 mL) in 15 mL of methanol was heated at reflux for 10 min to give 70% N-(2-chloro-3,4-dimethoxybenzylideneamino)guanidine acetate. N-(5-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate in vitro showed the binding affinity to MC1, MC3, MC4, and MC5 receptor with  $K_i$  of 6.4, 1, 17.1, and 8.7  $\mu\text{M}$ , resp.

ST benzylideneaminoguanidine benzylideneaminohydroxyguanidine prepn **melanocortin** receptor ligand; disorder **melanocortin** system benzylideneaminohydroxyguanidine prepn; inflammation benzylideneaminohydroxyguanidine prepn; mental disorder benzylideneaminohydroxyguanidine prepn; sexual function benzylideneaminohydroxyguanidine prepn; allergy treatment benzylideneaminohydroxyguanidine prepn; cardiovascular system disorder treatment benzylideneaminohydroxyguanidine prepn; pain diabetes type II treatment benzylideneaminohydroxyguanidine prepn; obesity treatment benzylideneaminohydroxyguanidine prepn; anorexia treatment benzylideneaminohydroxyguanidine prepn

IT Diagnosis  
(agents, for melanoma or cancer metastasis; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Melanoma  
(anticancer and diagnostic agents for; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT Nervous system  
(central, degeneration; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for

- treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Neoplasm  
(diagnostic agents for; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Blood  
Endocrine system  
Lymph node  
(disease; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Sexual behavior  
(disorder; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Hormones, animal, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(disorders; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Pituitary hormone receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**melanocortin**; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Antitumor agents  
(melanoma; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Neoplasm  
(metastasis, diagnostic agents for; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Regeneration, animal  
(nerve, peripheral; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Diabetes mellitus  
(non-insulin-dependent; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)
- IT Allergy inhibitors  
Analgesics  
Anorexia  
Anti-inflammatory agents  
Antiobesity agents  
Cardiovascular agents  
Ischemia  
Mental disorder  
Reperfusion

## Skin, disease

(prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

## IT Cosmetics

(skin-lightening; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

## IT Skin

(tanning inducers; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT 128908-32-7P, **Melanocortin**

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as **melanocortin** receptor ligands for treatment of disorders of **melanocortin** system or dysfunctions of endocrine or hormonal system)

IT 25054-35-7P, N-(2,4-Dinitrobenzylideneamino)guanidine acetate  
 65565-57-3P, N-(Benzylideneamino)guanidine acetate 85894-20-8P,  
 N-(3-Iodobenzylideneamino)-N'-hydroxyguanidine tosylate 87861-89-0P,  
 N-(3-Methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 96826-46-9P,  
 N-(3-Nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 96826-48-1P,  
 N-(4-Cyanobenzylideneamino)-N'-hydroxyguanidine tosylate 96826-50-5P,  
 N-(4-Chloro-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate  
 96826-65-2P, N-(2,5-Dimethoxybenzylideneamino)-N'-hydroxyguanidine  
 tosylate 123541-21-9P, N-(2,3,4-Trihydroxybenzylideneamino)-N'-  
 hydroxyguanidine tosylate 123541-25-3P, N-(2-Hydroxybenzylideneamino)-N'-  
 hydroxyguanidine tosylate 131610-93-0P, N-(2,4-  
 Dihydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 131610-95-2P,  
 N-(2-Hydroxy-4-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate  
 131610-97-4P, N-(2-Hydroxy-4,6-dimethoxybenzylideneamino)-N'-  
 hydroxyguanidine tosylate 131610-99-6P, N-(2-Hydroxy-5-  
 nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 131611-00-2P,  
 N-(Benzylideneamino)-N'-hydroxyguanidine tosylate 139613-32-4P,  
 N-(3-Fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 139613-44-8P,  
 N-(3-Hydroxy-4-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate  
 148796-78-5P, N-(5-Bromo-2-hydroxybenzylideneamino)-N'-hydroxyguanidine  
 tosylate 160486-31-7P, N-(4-Dimethylaminobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 160916-41-6P, N-(4-Methoxybenzylideneamino)-N'-  
 hydroxyguanidine tosylate 161016-41-7P, N-(3,4-  
 Methylenedioxybenzylideneamino)-N'-hydroxyguanidine tosylate  
 161016-43-9P, N-(2,3,4-Trimethoxybenzylideneamino)-N'-hydroxyguanidine  
 tosylate 161016-44-0P, N-(2,4,5-Trimethoxybenzylideneamino)-N'-  
 hydroxyguanidine 161016-45-1P, N-(2,4,5-Trimethoxybenzylideneamino)-N'-  
 hydroxyguanidine tosylate 161016-47-3P, N-(2,4,6-  
 Trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 161016-49-5P,  
 N-(3,4,5-Trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate  
 170996-62-0P, N-(3-Bromo-4-methoxybenzylideneamino)guanidine hydrochloride  
 208582-89-2P, N-(3,4-Dimethoxy-2-chlorobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 208583-03-3P, N-(3-Bromo-4-  
 methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 219924-72-8P,  
 N-(2-Sulfobenzylideneamino)-N'-hydroxyguanidine 284042-43-9P,  
 N-(3,4-Dimethoxy-2-chlorobenzylideneamino)guanidine 332395-03-6P  
 332395-39-8P, N-(2-Chloro-3,4-dimethoxybenzylideneamino)guanidine acetate

332395-47-8P, N-(3,4,5-Trimethoxybenzylideneamino)guanidine acetate  
 332395-48-9P, N-(2,4,6-Trimethoxybenzylideneamino)guanidine acetate  
 332395-49-0P, N-(3-Nitrobenzylideneamino)guanidine acetate 332395-50-3P,  
 N-(2-Hydroxy-4,6-dimethoxybenzylideneamino)guanidine acetate  
 332395-51-4P, N-(4-Nitrobenzylideneamino)guanidine acetate 332395-52-5P,  
 N-(3-Bromo-4-fluorobenzylideneamino)guanidine acetate 332395-53-6P,  
 N-(2,3-Difluorobenzylideneamino)guanidine acetate 332395-54-7P,  
 N-(4-Chloro-3-fluorobenzylideneamino)guanidine acetate 332395-55-8P,  
 N-(3-Methoxy-2,6-dinitrobenzylideneamino)guanidine hydrochloride  
 332395-56-9P, N-(3-Bromo-2,6-dinitrobenzylideneamino)guanidine  
 hydrochloride 332395-57-0P, N-(2,3-Dimethoxy-5,6-  
 dinitrobenzylideneamino)guanidine acetate 332395-58-1P,  
 N-(5-Bromo-2,4-dimethoxybenzylideneamino)guanidine acetate 332395-59-2P,  
 N-(2,3-Dimethoxy-5-nitrobenzylideneamino)guanidine acetate 332395-60-5P,  
 N-(4-Phenylbenzylideneamino)guanidine acetate 332395-61-6P,  
 N-(3,4-Difluorobenzylideneamino)guanidine acetate 332395-62-7P,  
 N-(2-Fluoro-5-nitrobenzylideneamino)guanidine acetate 332395-63-8P,  
 N-(4-Bromo-2-fluorobenzylideneamino)guanidine acetate 332395-64-9P,  
 N-(3,5-Dichlorobenzylideneamino)guanidine acetate 332395-65-0P,  
 N-(3,5-Dinitrobenzylideneamino)guanidine acetate 332395-66-1P,  
 N-(2,6-Difluorobenzylideneamino)guanidine acetate 332395-67-2P,  
 N-(3-Chloro-4-fluorobenzylideneamino)guanidine acetate 332395-68-3P,  
 N-(2-Bromo-4-nitrobenzylideneamino)guanidine acetate 332395-69-4P,  
 N-(2-Bromo-5-nitrobenzylideneamino)guanidine acetate 332395-70-7P,  
 N-(2-Iodobenzylideneamino)guanidine acetate 332395-71-8P,  
 N-(2,3-Dimethoxy-5-nitrobenzylideneamino)guanidine hydrochloride  
 332395-72-9P, N-(2-Hydroxy-4-methoxybenzylideneamino)guanidine acetate  
 332395-73-0P, N-(4-Bromo-3-nitrobenzylideneamino)guanidine acetate  
 332395-74-1P, N-(6-Chloro-2,3-dinitrobenzylideneamino)guanidine  
 hydrochloride 332395-75-2P, N-(3-Iodobenzylideneamino)guanidine  
 hydrochloride 332395-76-3P, N-(2-Sulfobenzylideneamino)guanidine  
 hydrochloride 332395-77-4P, N-(3,4-Dichlorobenzylideneamino)guanidine  
 acetate 332395-78-5P, N-(2-Chloro-5-nitrobenzylideneamino)guanidine  
 acetate 332395-79-6P, N-(4-Chloro-3-nitrobenzylideneamino)guanidine  
 acetate 332395-80-9P, N-(4-Fluoro-3-nitrobenzylideneamino)guanidine  
 acetate 332395-81-0P, N-(4-Methoxy-3-nitrobenzylideneamino)guanidine  
 acetate 332395-83-2P, N-(3,5-Dichloro-2-nitrobenzylideneamino)guanidine  
 acetate 332395-84-3P, N-(2-Hydroxy-3-methoxy-5-  
 nitrobenzylideneamino)guanidine hydrochloride 332395-85-4P,  
 N-(2-Hydroxy-4-methoxy-5-nitrobenzylideneamino)guanidine hemiacetate  
 332395-86-5P, N-(3-Chloro-4-methoxy-5-nitrobenzylideneamino)guanidine  
 acetate 332395-87-6P, N-(3,5-Dichloro-4-methoxybenzylideneamino)guanidin  
 e acetate 332395-88-7P, N-(3-Bromo-4-methoxy-5-  
 methylbenzylideneamino)guanidine acetate 332395-89-8P,  
 N-(2,3,4-Trimethoxybenzylideneamino)guanidine hydrochloride  
 332395-90-1P, N-(4-Chloro-2-methoxy-5-nitrobenzylideneamino)guanidine  
 acetate 332395-91-2P, N-(3,6-Dichloro-2-nitrobenzylideneamino)guanidine  
 acetate 332395-92-3P, N-(2-Hydroxy-4-methyl-5-  
 nitrobenzylideneamino)guanidine hydrochloride 332395-93-4P,  
 N-(2-Bromo-5-chloro-3-nitrobenzylideneamino)guanidine acetate  
 332395-94-5P, N-(3-Hydroxy-4-methyl-2-nitrobenzylideneamino)guanidine  
 acetate 332395-95-6P, N-(5-Bromo-4-methyl-2-  
 nitrobenzylideneamino)guanidine hydrochloride 332395-96-7P,  
 N-(5-Bromo-2-hydroxy-3-nitrobenzylideneamino)guanidine hydrochloride  
 332395-97-8P, N-(5-Bromo-2-methoxy-3-nitrobenzylideneamino)guanidine  
 hydrochloride 332395-98-9P, N-(2,4-Dimethoxy-5-  
 nitrobenzylideneamino)guanidine acetate 332395-99-0P,  
 N-(4-Bromo-2-fluoro-5-nitrobenzylideneamino)guanidine acetate  
 398134-07-1P, N-(3-Bromobenzylideneamino)-N'-hydroxyguanidine tosylate  
 398134-09-3P, N-(5-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine

tosylate 398134-12-8P, N-(2,3-Dihydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-14-0P, N-(4,5-Methylenedioxy-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-16-2P, N-(2-Bromobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-18-4P, N-(2,3-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-20-8P, N-(2,5-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-22-0P, N-(4-Nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-24-2P, N-(2-Hydroxy-3-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-26-4P, N-(3-Chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-28-6P, N-(2,3,4-Tribenzyloxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-30-0P, N-(4-Chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-31-1P, N-(4-Bromobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-33-3P, N-(4-Diethylaminobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-35-5P, N-(4-Hydroxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-37-7P, N-(2-Nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-39-9P, N-(2-Bromo-3,4,5-trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-41-3P, N-(2,4-Dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-43-5P, N-(2-Chloro-6-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-45-7P, N-(3,5-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-47-9P, N-(5-Hydroxy-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-49-1P, N-(3,6-Dimethoxy-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-51-5P, N-(2,3-Dimethoxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-53-7P, N-(2,3-Dimethoxy-5,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-55-9P, N-(2,6-Dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-57-1P, N-(2,3-Dimethoxy-6-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-58-2P, N-(5-Bromo-2,4-dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-59-3P, N-(5-Bromo-2,4-dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-61-7P, N-(2-Fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-63-9P, N-(2-Methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-65-1P, N-(2,3-Methylenedioxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-67-3P, N-(4-Bromo-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-69-5P, N-(5-Bromo-2-hydroxy-3-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398134-71-9P, N-(2,3-Dinitro-6-chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-73-1P, N-(3,6-Dichloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-75-3P, N-(2,6-Dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-77-5P, N-(2-Chloro-3,4-dimethoxy-6-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-79-7P, N-(2-Chlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-81-1P, N-(4-Fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-83-3P, N-(4-Fluoro-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-85-5P, N-(2-Chloro-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-87-7P, N-(4-Chloro-2-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-89-9P, N-(3,4-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-91-3P, N-(2,4-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-93-5P, N-(4-Methoxy-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-95-7P, N-(2,3-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-97-9P, N-(2-Fluoro-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398134-99-1P, N-(2-Methoxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-01-8P, N-(4-Hydroxy-3,5-dimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-03-0P, N-(2-Bromo-5-chloro-3-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-05-2P, N-(3-Bromo-2,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-07-4P, N-(3,5-Dinitro-2-methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-09-6P, N-(5-Bromo-2-hydroxy-3-

nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-11-0P,  
 N-(3-Methoxy-2,6-dinitrobenzylideneamino)-N'-hydroxyguanidine tosylate  
 398135-13-2P, N-(3-Bromo-4-fluorobenzylideneamino)-N'-hydroxyguanidine  
 tosylate 398135-15-4P, N-(2,3-Difluorobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-17-6P, N-(4-Chloro-3-  
 fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-19-8P,  
 N-(4-Bromo-3-fluorobenzylideneamino)-N'-hydroxyguanidine tosylate  
 398135-21-2P, N-(3,4-Difluorobenzylideneamino)-N'-hydroxyguanidine  
 tosylate 398135-23-4P, N-(4-Phenylbenzylideneamino)-N'-hydroxyguanidine  
 tosylate 398135-25-6P, N-(3-Chloro-2,6-dinitrobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-27-8P, N-(4-Bromo-2-  
 fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-29-0P,  
 N-(2-Bromo-5-nitrobenzylideneamino)-N'-hydroxyguanidine tosylate  
 398135-30-3P, N-(2,4-Dinitrobenzylideneamino)-N'-hydroxyguanidine  
 hydrochloride 398135-32-5P, N-(2,6-Difluorobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-34-7P, N-(3-Chloro-4-  
 fluorobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-36-9P,  
 N-(3,5-Dichlorobenzylideneamino)-N'-hydroxyguanidine tosylate  
 398135-38-1P, N-(2-Bromo-4-nitrobenzylideneamino)-N'-hydroxyguanidine  
 tosylate 398135-40-5P, N-(3,5-Dinitrobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-42-7P, N-(2,3-Dinitrobenzylideneamino)-  
 N'-hydroxyguanidine tosylate 398135-44-9P, N-(2-Iodobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-46-1P, N-(2-Chloro-3,4,5-  
 trimethoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-48-3P,  
 N-(3,5-Difluorobenzylideneamino)-N'-hydroxyguanidine tosylate  
 398135-50-7P, N-(5-Bromo-2,3,4-trimethoxybenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-52-9P, N-(3-Chloro-4-  
 methoxybenzylideneamino)-N'-hydroxyguanidine tosylate 398135-53-0P,  
 N-(2,3-Dimethoxy-5-nitrobenzylideneamino)-N'-hydroxyguanidine  
 hydrochloride 398135-55-2P, N-(3,5-Difluoro-2-nitrobenzylideneamino)-N'-  
 hydroxyguanidine tosylate 398135-57-4P, N-(3,5-Dichloro-2-  
 nitrobenzylideneamino)-N'-hydroxyguanidine tosylate 398135-58-5P,  
 N-(3,5-Difluoro-2-nitrobenzylideneamino)guanidine acetate 398135-59-6P  
 398135-60-9P 398135-61-0P 398135-62-1P 398135-63-2P 398135-64-3P  
 398135-65-4P 398135-66-5P 398135-67-6P 398135-68-7P 398135-69-8P  
 398135-70-1P 398135-71-2P 398135-72-3P 398135-73-4P 398135-74-5P  
 398135-75-6P 398135-76-7P 398135-77-8P 398135-78-9P 398135-79-0P  
 398135-81-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as  
**melanocortin** receptor ligands for treatment of disorders of  
**melanocortin** system or dysfunctions of endocrine or hormonal  
 system)

IT 2582-30-1, Aminoguanidine bicarbonate 5417-17-4, 2-Chloro-3,4-  
 dimethoxybenzaldehyde

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; prepn. of N-(benzylideneamino)-N'-hydroxyguanidines as  
**melanocortin** receptor ligands for treatment of disorders of  
**melanocortin** system or dysfunctions of endocrine or hormonal  
 system)

L20 ANSWER 5 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:96099 CA

TITLE: Treatment of male **sexual dysfunction**

INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn;  
 Wayman, Christopher Peter

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 124 pp.



CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003995	A2	20020117	WO 2001-IB1187	20010702
WO 2002003995	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002052370	A1	20020502	US 2001-893585	20010628
PRIORITY APPLN. INFO.:			GB 2000-16684	A 20000706
			GB 2000-30647	A 20001215
			GB 2001-6167	A 20010313
			GB 2001-8483	A 20010404
			US 2000-219100P	P 20000718
			GB 2001-1584	A 20010122
			US 2001-274957P	P 20010312

OTHER SOURCE(S): MARPAT 136:96099

AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male **sexual dysfunction**, in particular MED.

TI Treatment of male **sexual dysfunction**

AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male **sexual dysfunction**, in particular MED.

ST male **sexual dysfunction** neutral endopeptidase inhibitor

IT Opioid receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (ORL1, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Neuropeptide Y receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Y5, antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT Neuropeptide Y receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (Y1, antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

IT VIP receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (agonists; treatment of male **sexual dysfunction**)

- using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Endothelin receptors  
Tachykinin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Estrogens  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antiestrogens; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Ion channel blockers  
(calcium; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Sexual behavior  
(disorder, male; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Transport proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(dopamine-transporting, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Sexual behavior  
(ejaculation, disorder; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Alkaloids, biological studies  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ergot; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Anticholesteremic agents  
(fibrates and statins; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Sexual behavior  
(impotence; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Pituitary hormone receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**melanocortin**, agonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

- IT Cannabinoid receptors
  - Estrogen receptors
  - Opioid receptors
  - Oxytocin receptors
  - Vasopressin receptors
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Transport proteins
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (norepinephrine-transporting, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Drug delivery systems
  - (oral; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Ion channel openers
  - (potassium; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Sexual behavior
  - (premature ejaculation; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Transport proteins
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
    - (serotonin-transporting, modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Drug delivery systems
  - (tablets; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 5-HT agonists
  - 5-HT antagonists
  - Angiotensin receptor antagonists
  - Anticoagulants
  - Dopamine agonists
  - Drug interactions
  - Drug screening
  - Opioid antagonists
  - Platelet aggregation inhibitors
  - Purinoceptor agonists
  - Vasodilators
    - (treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT Estrogens
  - Opioids

## Prostaglandins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT Adrenoceptor antagonists

(.alpha.-; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 57576-52-0, Thromboxane A2

RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 82785-45-3, Neuropeptide Y

RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 10102-43-9, Nitric oxide, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (donors and agonists; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 128908-32-7, Melanocortin

RL: BSU (Biological study, unclassified); BIOL (Biological study) (enhancers; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 9028-35-7, HMG-CoA reductase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, statins; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 9000-81-1, Acetylcholinesterase 9040-59-9, Phosphodiesterase II 9068-52-4, Phosphodiesterase V 82707-54-8, Neutral endopeptidase 138238-81-0, Endothelin converting enzyme

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 9036-21-9, Phosphodiesterase 8

RL: BSU (Biological study, unclassified); BIOL (Biological study) (isoforms, inhibitors; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

## IT 9088-07-7, Natriuretic factor 85637-73-6, Atrial natriuretic factor

RL: BSU (Biological study, unclassified); BIOL (Biological study) (modulators; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with

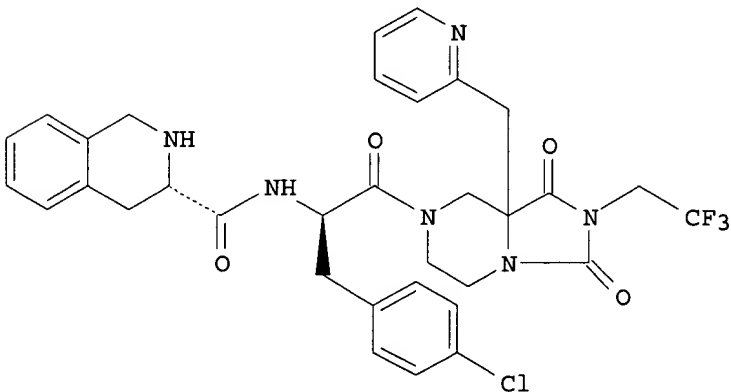
- phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (sensitizing agents; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 125978-95-2, Nitric oxide synthase  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (substrates; treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 9015-82-1, Angiotensin converting enzyme  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 337962-68-2P 337962-69-3P 337962-70-6P 337962-71-7P 337962-72-8P 337962-73-9P 337962-74-0P 388630-36-2P 388630-55-5P  
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 58-22-0, Testosterone 71-58-9, Medroxyprogesterone acetate 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 37221-79-7, Vasoactive intestinal peptide 37221-79-7D, Vasoactive intestinal peptide, analogs 139755-83-2, Sildenafil 147676-53-7 171596-29-5, IC-351 215297-27-1 224785-90-4, Vardenafil 334826-98-1 334827-47-3 334827-59-7 335077-64-0 335077-70-8 389128-36-3  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 98-10-2, Benzenesulfonamide 108-33-8, 2-Amino-5-methyl-1,3,4-thiadiazole 7663-77-6, N-(3-Aminopropyl)-2-pyrrolidinone 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole 59892-44-3 118755-30-9 118755-86-5 118756-03-9 118783-85-0 118786-35-9 136834-71-4 136834-85-0 136850-24-3  
RL: RCT (Reactant); RACT (Reactant or reagent) (treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
- IT 337962-78-4P 337962-79-5P 337962-80-8P 337962-81-9P 337962-83-1P 337962-84-2P 337962-91-1P 337962-93-3P 388630-52-2P 388630-83-9P 388631-26-3P 388631-29-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (treatment of male **sexual dysfunction** using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

09/990,499

IT 388630-37-3P 388630-54-4P 389083-04-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(treatment of male **sexual dysfunction** using neutral  
endopeptidase inhibitors and their combination with phosphodiesterase  
type 5 inhibitors and other agents in relation to inhibition of  
angiotensin converting enzyme)

L20 ANSWER 6 OF 16 CA COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 136:69824 CA  
TITLE: Preparation of heterocycle compounds as  
**melanocortin** receptor ligands  
INVENTOR(S): Carpino, Philip Albert; Cole, Bridget McCarthy;  
Morgan, Bradley Paul  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 108 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000654	A1	20020103	WO 2001-IB995	20010531
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001060548	A5	20020108	AU 2001-60548	20010531
US 2002072604	A1	20020613	US 2001-891026	20010625
PRIORITY APPLN. INFO.:			US 2000-214616P	P 20000628
			WO 2001-IB995	W 20010531
OTHER SOURCE(S):	MARPAT 136:69824			
GI				



II

AB Compds. represented by formula HET-COCR3R4-NX4-CO(CR6R7)m-D [I; wherein m = 0, 1 or 2; HET = heterocyclyl; R3, R4 = H,, C1-8 alkyl, CH(R8)-aryl, -CH(R8)-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl (wherein the aryl or heteroaryl groups are optionally substituted by one or two groups; R8 = H, C1-8 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, -C3-6 cycloalkyl); R6, R7 = H, C1-6 alkyl, -C0-3 alkyl-aryl, -C0-3 alkyl-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl; or R6 and R7 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally contg. an addnl. heteroatom selected from O, S, NR3; D = -C0-6 alkylamino-C(:NR7)-NR15R16, -C0-6 alkylaminopyridyl, -C0-6 alkylaminoimidazolyl, -C0-6 alkylaminothiazolyl, -C0-6 alkylaminopyrimidinyl, -C0-6 alkylaminopiperazinyl-R15, -C0-6 alkylmorpholinyl, etc. (wherein R15, R16 = H, -C1-6 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, or -C0-3 alkyl-C3-8 cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two groups); X4 = H or C1-6 alkyl or X4 is taken together with R4 and the nitrogen atom to which X4 is attached and the carbon atom to which R4 is attached and form a five to seven membered ring] are prepd. Melanocortins are peptides derived from pro-opiomelanocortins (POMC) that bind to and activate G-protein coupled receptors (GPCR's) of the **melanocortin** receptor family and regulate a diverse no. of physiol. processes including food intake., metab., and thermogenesis as well as **sexual dysfunction**. These compds. I are useful for the treatment or prevention of disorders, diseases, or conditions responsive to the activation of **melanocortin** receptor including obesity, diabetes mellitus, male or female **sexual dysfunction**, erectile dysfunction, or disorders that cause redn. in appetite, or feeding behavior and/or body wt.; for modulating appetite and metabolic rates; for acutely stimulating the appetite for the treatment of hepatic lipidosis, cachexia, and other pathologies resulting in/from inappropriate food intake and wt. loss; for acutely stimulating the appetite of livestock for the treatment of ketosis, postpartum anestrus, and other metabolic and reproductive pathologies resulting in/from inappropriate food intake and wt. loss; and for enhancing growth and survivability of neonates in livestock. Thus, esterification of N-Boc-L-Tic-OH with N-hydroxysuccinimide using Et3N and EDC in CH2Cl2 at room temp. for 4 h gave 3,4-Dihydro-1H-isoquinoline-2,3-(S)-dicarboxylic acid 2-tert-Bu ester 3-(2,5-dioxopyrrolidin-1-yl) ester which was condensed with D-p-chlorophenylalanine in the presence of Et3N in CH2Cl2 at room temp. overnight to give 3-(S)-[(R)-1-Carboxy-2-(4-chlorophenyl)ethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester. The latter compd. was further condensed with 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione using Et3N and EDC in CH2Cl2 at 0.degree. for 5 h to give (S)-3-[(R)-1-(4-Chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester which was treated with a mixt. of EtOH and concd. HCl at 0.degree. for 0.5 h to give (S)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid N-[(R)-1-(4-chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl]amide (II) hydrochloride which may be considered as a dipeptide analog heptercycle amide, N-[N-(L-1,2,3,4-Tetrahydroisoquinoline-3-carbonyl)-D-p-chlorophenylalanyl]-1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of heterocycle compounds as **melanocortin** receptor ligands

AB Compds. represented by formula HET-COCR3R4-NX4-CO(CR6R7)m-D [I; wherein m = 0, 1 or 2; HET = heterocyclyl; R3, R4 = H,, C1-8 alkyl, CH(R8)-aryl,

-CH(R8)-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl (wherein the aryl or heteroaryl groups are optionally substituted by one or two groups; R8 = H, C1-8 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, -C3-6 cycloalkyl); R6, R7 = H, C1-6 alkyl, -C0-3 alkyl-aryl, -C0-3 alkyl-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl; or R6 and R7 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally contg. an addnl. heteroatom selected from O, S, NR3; D = -C0-6 alkylamino-C(:NR7)-NR15R16, -C0-6 alkylaminopyridyl, -C0-6 alkylaminoimidazolyl, -C0-6 alkylaminothiazolyl, -C0-6 alkylaminopyrimidinyl, -C0-6 alkylaminopiperazinyl-R15, -C0-6 alkylmorpholinyl, etc. (wherein R15, R16 = H, -C1-6 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, or -C0-3 alkyl-C3-8 cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two groups); X4 = H or C1-6 alkyl or X4 is taken together with R4 and the nitrogen atom to which X4 is attached and the carbon atom to which R4 is attached and form a five to seven membered ring] are prepd. Melanocortins are peptides derived from pro-opiomelanocortins (POMC) that bind to and activate G-protein coupled receptors (GPCR's) of the **melanocortin** receptor family and regulate a diverse no. of physiol. processes including food intake., metab., and thermogenesis as well as **sexual dysfunction**

. These compds. I are useful for the treatment or prevention of disorders, diseases, or conditions responsive to the activation of **melanocortin** receptor including obesity, diabetes mellitus, male or female **sexual dysfunction**, erectile dysfunction, or disorders that cause redn. in appetite, or feeding behavior and/or body wt.; for modulating appetite and metabolic rates; for acutely stimulating the appetite for the treatment of hepatic lipidosis, cachexia, and other pathologies resulting in/from inappropriate food intake and wt. loss; for acutely stimulating the appetite of livestock for the treatment of ketosis, postpartum anestrus, and other metabolic and reproductive pathologies resulting in/from inappropriate food intake and wt. loss; and for enhancing growth and survivability of neonates in livestock. Thus, esterification of N-Boc-L-Tic-OH with N-hydroxysuccinimide using Et3N and EDC in CH2Cl2 at room temp. for 4 h gave 3,4-Dihydro-1H-isoquinoline-2,3-(S)-dicarboxylic acid 2-tert-Bu ester 3-(2,5-dioxopyrrolidin-1-yl) ester which was condensed with D-p-chlorophenylalanine in the presence of Et3N in CH2Cl2 at room temp. overnight to give 3-(S)-[(R)-1-Carboxy-2-(4-chlorophenyl)ethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester. The latter compd. was further condensed with 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione using Et3N and EDC in CH2Cl2 at 0.degree. for 5 h to give (S)-3-[(R)-1-(4-Chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester which was treated with a mixt. of EtOH and concd. HCl at 0.degree. for 0.5 h to give (S)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid N-[(R)-1-(4-chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl]amide (II) hydrochloride which may be considered as a dipeptide analog heptercycle amide, N-[N-(L-1,2,3,4-Tetrahydroisoquinoline-3-carbonyl)-D-p-chlorophenylalanyl]-1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazine.

- ST heterocyclic compd prepn prevention treatment obesity;  
**melanocortin** receptor ligand tetrahydroisoquinolinecarboxamide  
 prepn; imidazopyrazine prepn prevention treatment diabetes mellitus  
**sexual dysfunction**; appetite metabolic rate modulator  
 heterocyclic compd prepn; tetrahydroisoquinolinecarbonylchlorophenylalanin  
 e prepn dipeptide analog heterocycle amide
- IT Peptides, preparation  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU



(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amides, dipeptide analog heterocycle amides; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Sexual behavior

(disorder; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Sexual behavior

(impotence; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Ketone bodies

(ketosis, livestock, appetite stimulants in treatment of; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Lipids, processes

RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
(lipidosis, livestock, appetite stimulants in treatment of; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Newborn

(livestock, enhancers for growth and survivability; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Body weight

(loss; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Pituitary hormone receptors

RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
(**melanocortin**; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Appetite

Metabolism, animal

(modulators; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Antidiabetic agents

Antiobesity agents

Cachexia

(prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT Heterocyclic compounds

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT 252008-71-2P 252008-73-4P 384345-09-9P 384345-10-2P 384345-12-4P  
384345-13-5P 384345-15-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT 384345-08-8P 384345-11-3P 384345-14-6P 384345-16-8P 384345-17-9P  
384345-21-5P 384345-22-6P 384345-23-7P 384345-24-8P 384345-25-9P  
384345-26-0P 384345-27-1P 384345-28-2P 384345-29-3P 384345-30-6P  
384345-31-7P 384345-32-8P 384345-33-9P 384345-34-0P 384345-35-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

IT 6066-82-6, N-Hydroxysuccinimide 14091-08-8, D-p-Chlorophenylalanine  
78879-20-6, N-Boc-L-Tic-OH 115962-35-1, N-Boc-D-Tic-OH 193274-04-3,  
3a-Benzyl-2-methyl-2,3a,4,5,6,7-hexahydropyrazolo[4,3-c]pyridin-3-one  
218952-63-7, 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; prepn. of heterocycle compds. as **melanocortin** receptor ligands and therapeutic agents for treatment of prevention of obesity, diabetes mellitus, male or female **sexual dysfunction**)

L20 ANSWER 7 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:15253 CA

TITLE: **Melanocortin** receptor agonists, and preparation thereof, for therapeutic use

INVENTOR(S): Bakshi, Raman Kumar; Nargund, Ravi P.; Ye, Zhixiong

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

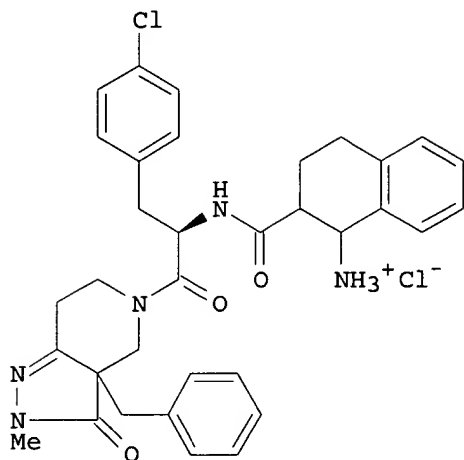
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091752	A1	20011206	WO 2001-US17014	20010525
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002004512	A1	20020110	US 2001-867309	20010529

US 6376509 B2 20020423  
 PRIORITY APPLN. INFO.: US 2000-207918P P 20000530  
 OTHER SOURCE(S): MARPAT 136:15253  
 GI



I

AB The invention discloses compds. and derivs. thereof which are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin-4** receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, e.g. obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**.  
 Prepn. of e.g. I is described.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Melanocortin** receptor agonists, and preparation thereof, for therapeutic use

AB The invention discloses compds. and derivs. thereof which are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin-4** receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, e.g. obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**.  
 Prepn. of e.g. I is described.

ST **melanocortin** 4 receptor agonist prepn therapeutic; obesity diabetes treatment **melanocortin** receptor agonist; **sexual dysfunction** treatment **melanocortin** receptor agonist; erectile dysfunction treatment **melanocortin** receptor agonist

IT Drug delivery systems  
 (capsules; **melanocortin** receptor agonist prepn. for therapeutic use)

IT Anticholesteremic agents  
 (cholesterol sequestrants; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)

IT Sexual behavior  
 (disorder; **melanocortin** receptor agonist prepn. for therapeutic use)

- IT Sequestering agents  
(for cholesterol; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT Sexual behavior  
(impotence; **melanocortin** receptor agonist prepn. for therapeutic use)
- IT Pituitary hormone receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**melanocortin** 4; **melanocortin** receptor agonist prepn. for therapeutic use)
- IT Antidiabetic agents  
Antiobesity agents  
Drug delivery systems  
(**melanocortin** receptor agonist prepn. for therapeutic use)
- IT Dopamine agonists  
(**melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT Sulfonylureas  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT Pituitary hormone receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**melanocortin**; **melanocortin** receptor agonist prepn. for therapeutic use)
- IT Adrenoceptor antagonists  
(.alpha.2-; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT Adrenoceptor agonists  
(.beta.3-; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT 82785-45-3, Neuropeptide Y  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antagonists; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT 9001-42-7, .alpha.-Glucosidase 9028-35-7, HMG-CoA reductase 9068-52-4, Phosphodiesterase V  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; **melanocortin** receptor agonist prepn. for therapeutic use, and use with other agents)
- IT 378741-82-3P 379266-73-6DP, isomers 379266-73-6P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**melanocortin** receptor agonist prepn. for therapeutic use)
- IT 378741-76-5 379266-96-3  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**melanocortin** receptor agonist prepn. for therapeutic use)
- IT 59433-90-8P 378741-77-6P 378741-78-7P 378741-79-8P 378741-80-1P 379266-72-5DP, isomers 379266-72-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and reaction; **melanocortin** receptor agonist prepn. for therapeutic use)
- IT 447-53-0, 1,2-Dihydronaphthalene 1189-71-5, Chlorosulfonyl isocyanate 24424-99-5 57292-44-1 115962-35-1 193274-04-3 378741-81-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction; **melanocortin** receptor agonist prepn. for

therapeutic use)

IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(sensitizers and mimetics; **melanocortin** receptor agonist

prepn. for therapeutic use, and use with other agents)

L20 ANSWER 8 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 135:314399 CA

TITLE: Detection of variations in the DNA methylation profile  
of genes in the determining the risk of disease

INVENTOR(S): Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander

PATENT ASSIGNEE(S): Epigenomics A.-G., Germany

SOURCE: PCT Int. Appl., 636 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 68

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077373	A2	20011018	WO 2001-DE1486	20010406
W:				
			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,	
			CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,	
			ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,	
			LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,	
			SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,	
			ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:				
			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,	
			DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,	
			BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
DE 10019058	A1	20011220	DE 2000-10019058	20000406
WO 2001077373	A2	20011018	WO 2001-XA1486	20010406
W:				
			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,	
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			ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,	
			LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,	
			SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA,	
			ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:				
			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,	
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WO 2001077373	A2	20011018	WO 2001-XB1486	20010406
W:				
			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,	
			CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,	
			ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,	
			LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,	
			SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA,	
			ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:				
			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,	
			DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,	
			CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG	
WO 2001077373	A2	20011018	WO 2001-XC1486	20010406
W:				
			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,	
			CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,	
			ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,	
			LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,	
			SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA,	
			ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:				
			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,	

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DE 2000-10019058 A 20000406

WO 2001-DE1486 W 20010406

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or **sexual dysfunction**. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or **sexual dysfunction**. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

IT Pituitary hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**melanocortin** 4, detection of methylation in gene for;

detection of variations in DNA methylation profile of genes in detg. risk of disease)

L20 ANSWER 9 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 135:272990 CA

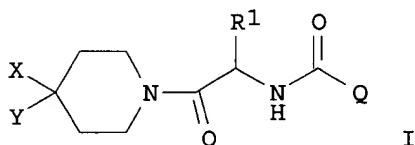
TITLE: Preparation of piperazinylcarbonylaminomethylcarbonylp  
iperidines as **melanocortin**-4 receptor  
agonists

INVENTOR(S): Palucki, Brenda L.; Barakat, Khaled J.; Guo, Liangqin;  
Lai, Yingjie; Nargund, Ravi P.; Park, Min K.; Pollard,  
Patrick G.; Sebhat, Iyassu K.; Ye, Zhixiong

09/990,499

PATENT ASSIGNEE(S): Merck + Co., Inc., USA  
SOURCE: PCT Int. Appl., 220 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070708	A1	20010927	WO 2001-US8935	20010320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002019523	A1	20020214	US 2001-812965	20010320
PRIORITY APPLN. INFO.:			US 2000-191442P	P 20000323
			US 2000-242265P	P 20001020
OTHER SOURCE(S):			MARPAT 135:272990	
GI				



AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepd. as **melanocortin-4** receptor (MC-4R) agonists. Thus, capsule formulations contg. title compd. (II) were prepd. Representative I activated MC-4R with IC50<1 .mu.M. I are claimed for the treatment of obesity, diabetes, and **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists

AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepd. as **melanocortin-4** receptor (MC-4R) agonists. Thus, capsule formulations contg. title compd. (II) were prepd. Representative

I activated MC-4R with  $IC_{50} < 1 \text{ } \mu\text{M}$ . I are claimed for the treatment of obesity, diabetes, and **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

ST piperazinylcarbonylaminomethylcarbonylpiperidine prepn  
**melanocortin** receptor agonist; **sexual dysfunction** treatment piperazinylcarbonylaminomethylcarbonylpiperidine; obesity treatment piperazinylcarbonylaminomethylcarbonylpiperidine; diabetes treatment piperazinylcarbonylaminomethylcarbonylpiperidine; piperidine piperazinylcarbonylaminomethylcarbonyl prepn  
**melanocortin** receptor agonist

IT Dopamine agonists  
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Sulfonylureas  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Sexual behavior  
(disorder, treatment; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Sexual behavior  
(impotence, treatment; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Pituitary hormone receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
(**melanocortin 4**, agonists; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Antidiabetic agents  
Antiobesity agents  
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Adrenoceptor antagonists  
(.alpha.2-, combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT Adrenoceptor agonists  
(.beta.3-, combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT 171596-29-5, IC-351 171599-83-0, Sildenafil citrate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT 363187-87-5P 363189-64-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT 363187-28-4P 363187-29-5P 363187-30-8P 363187-31-9P 363187-32-0P  
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363187-43-3P 363187-44-4P 363187-45-5P 363187-46-6P 363187-47-7P  
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363187-63-7P 363187-64-8P 363187-65-9P 363187-66-0P 363187-67-1P  
363187-68-2P 363187-69-3P 363187-70-6P 363187-71-7P 363187-72-8P



363187-73-9P	363187-74-0P	363187-75-1P	363187-76-2P	363187-77-3P
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363187-83-1P	363187-84-2P	363187-85-3P	363187-86-4P	363187-88-6P
363187-89-7P	363187-90-0P	363187-91-1P	363187-92-2P	363187-93-3P
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363188-59-4P	363188-60-7P	363188-61-8P	363188-62-9P	363188-63-0P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists)

IT	363190-17-4P	363190-19-6P	363190-59-4P	363190-60-7P	363190-61-8P
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	363190-67-4P	363190-68-5P	363190-69-6P	363190-70-9P	363190-71-0P
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363620-36-4P	363620-38-6P	363620-40-0P	363620-41-1P	363620-43-3P
363620-45-5P				

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT 75-44-5, Phosgene 75-64-9, tert-Butylamine, reactions 95-89-6, 3-Chloro-2,5-dimethylpyrazine 110-85-0, Piperazine, reactions 124-68-5 535-11-5, Ethyl 2-bromopropionate 556-82-1, 3-Methyl-2-buten-1-ol 565-69-5, Ethyl isopropyl ketone 598-21-0 811-93-8, 1,2-Diamino-2-methylpropane 1067-74-9, Methyl diethylphosphonoacetate 1193-18-6 1436-59-5, cis-1,2-Diaminocyclohexane 2749-11-3, (S)-2-Amino-1-propanol 3674-13-3, Ethyl 2,3-dibromopropionate 5521-55-1, 5-Methyl-2-pyrazinecarboxylic acid 5521-61-9, 6-Methyl-2-pyrazinecarboxylic acid 6294-40-2 7051-34-5, Cyclopropylmethyl bromide 7764-95-6 10316-79-7 20607-43-6, Sodium isopropylsulfide 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 29460-90-0, 2-Isopropylpyrazine 35761-26-3 45767-66-6, 2-Chloro-4-fluorobenzyl bromide 57292-44-1 57292-45-2 62234-36-0 69555-14-2 83949-32-0 84358-13-4 92329-61-8 129799-15-1 138775-02-7 138775-03-8 139631-62-2, Cyclopropylsulfonyl chloride 142851-03-4 312638-87-2 363192-22-7 363192-64-7 363192-65-8 363192-66-9 363192-73-8 363192-76-1 363192-79-4 363192-81-8 363192-86-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin-4** receptor agonists)

IT 2435-46-3P 19967-55-6P 29924-70-7P 35761-27-4P 96136-12-8P 126330-92-5P 167262-68-2P 252990-05-9P 278790-00-4P 363189-15-5P 363189-16-6P 363189-17-7P 363189-18-8P 363189-19-9P 363189-20-2P 363189-21-3P 363189-22-4P 363189-23-5P 363189-24-6P 363189-25-7P 363189-26-8P 363189-27-9P 363189-28-0P 363189-29-1P 363189-30-4P 363189-32-6P 363189-34-8P 363189-35-9P 363189-36-0P 363189-37-1P 363189-39-3P 363189-41-7P 363189-43-9P 363189-65-5P 363189-66-6P 363189-67-7P 363189-68-8P 363189-69-9P 363189-70-2P 363189-71-3P 363189-72-4P 363189-73-5P 363189-74-6P 363189-75-7P 363189-76-8P 363189-77-9P 363189-78-0P 363189-79-1P 363189-80-4P 363189-81-5P 363189-82-6P 363189-83-7P 363189-84-8P 363189-85-9P 363189-86-0P 363189-87-1P 363189-88-2P 363190-18-5P 363190-20-9P 363190-21-0P 363190-22-1P 363190-23-2P 363190-24-3P 363190-25-4P 363190-26-5P 363190-27-6P 363190-28-7P 363190-29-8P 363190-30-1P 363190-31-2P 363190-32-3P 363190-33-4P 363190-34-5P 363190-35-6P 363190-36-7P 363190-37-8P 363190-38-9P 363190-39-0P 363190-40-3P 363190-41-4P 363190-42-5P 363190-43-6P 363190-44-7P 363190-45-8P 363190-46-9P 363190-47-0P 363190-48-1P 363190-49-2P 363190-50-5P 363190-51-6P 363190-52-7P 363190-53-8P 363190-54-9P 363190-55-0P 363190-56-1P 363190-57-2P 363190-58-3P 363191-00-8P 363191-01-9P 363191-02-0P 363191-03-1P 363191-04-2P 363191-05-3P 363191-06-4P 363191-10-0P 363191-11-1P 363191-12-2P 363191-14-4P 363191-22-4P 363191-23-5P 363191-24-6P 363191-25-7P 363191-26-8P 363191-27-9P 363191-28-0P 363191-29-1P 363191-74-6P 363191-75-7P 363191-76-8P 363191-77-9P 363191-93-9P 363191-94-0P 363191-95-1P 363191-96-2P 363191-97-3P 363191-98-4P 363191-99-5P 363192-02-3P 363192-03-4P 363192-04-5P

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363620-42-2P				

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists)

L20 ANSWER 10 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 135:267270 CA

TITLE: Spiropiperidine derivatives as melanocortin receptor agonists

INVENTOR(S): Palucki, Brenda L.; Nargund, Ravi P.

PATENT ASSIGNEE(S): Merck + Co., Inc., USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

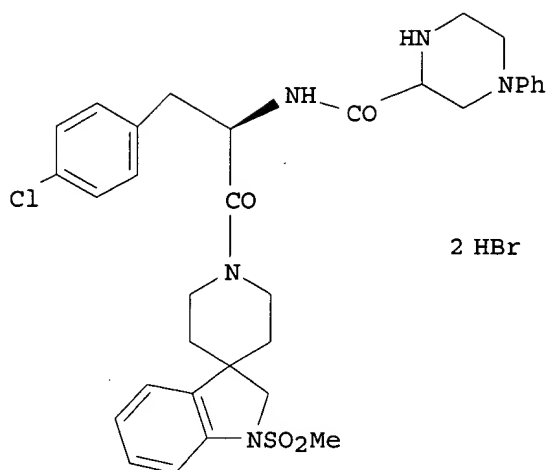
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070337	A1	20010927	WO 2001-US8833	20010320
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-191669P P 20000323

OTHER SOURCE(S): MARPAT 135:267270

GI



AB Certain novel spiroperidine derivs. are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin-4** receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. I was prepd. and pharmacol. tests are described.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Spiroperidine derivatives as **melanocortin** receptor agonists

AB Certain novel spiroperidine derivs. are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin-4** receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. I was prepd. and pharmacol. tests are described.

ST spiroperidine deriv prepn **melanocortin** receptor agonist

IT Sexual behavior  
(disorder; spiroperidine derivs. as **melanocortin** receptor agonists)

IT Sexual behavior  
(impotence; spiroperidine derivs. as **melanocortin** receptor agonists)

IT Pituitary hormone receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**melanocortin**; spiroperidine derivs. as **melanocortin** receptor agonists)

IT Antidiabetic agents  
Antiobesity agents  
(spiroperidine derivs. as **melanocortin** receptor agonists)

IT 128908-32-7, **Melanocortin**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(spiroperidine derivs. as **melanocortin** receptor agonists)

IT 126937-41-5 138775-03-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(spiroperidine derivs. as **melanocortin** receptor agonists)

IT 126937-42-6P 126937-43-7P 362513-36-8DP, acyl derivs. 362513-73-3P  
 362513-74-4P 362513-76-6P 362513-77-7P 362513-79-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 362513-35-7P 362513-36-8P 362513-37-9P 362513-38-0P 362513-39-1P  
 362513-40-4P 362513-41-5P 362513-42-6P 362513-43-7P 362513-44-8P  
 362513-45-9P 362513-46-0P 362513-47-1P 362513-48-2P 362513-49-3P  
 362513-50-6P 362513-51-7P 362513-52-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
 USES (Uses)  
 (spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 362513-53-9P 362513-54-0P 362513-55-1P 362513-56-2P 362513-57-3P  
 362513-58-4P 362513-59-5P 362513-60-8P 362513-61-9P 362513-62-0P  
 362513-63-1P 362513-64-2P 362513-65-3P 362513-66-4P 362513-67-5P  
 362513-68-6P 362513-69-7P 362513-70-0P 362513-71-1P 362513-72-2P  
 362513-78-8P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (spiropiperidine derivs. as **melanocortin** receptor agonists)

L20 ANSWER 11 OF 16 CA COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 135:205579 CA  
 TITLE: HP-3228 and related peptides to treat **sexual  
 dysfunction**  
 INVENTOR(S): Girtten, Beverly E.; Tuttle, Ronald R.  
 PATENT ASSIGNEE(S): Lion Bioscience A.-G., Germany  
 SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 306,686.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6284735	B1	20010904	US 1999-356386	19990716
US 6127381	A	20001003	US 1999-301391	19990428
WO 2001005401	A1	20010125	WO 2000-US19408	20000713
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1998-83368P P 19980428  
 US 1999-301391 A1 19990428  
 US 1999-306686 A2 19990506  
 US 1999-356386 A2 19990716  
 US 1999-364825 A2 19990730  
 US 1999-401004 A2 19990921

OTHER SOURCE(S): MARPAT 135:205579  
 AB Methods for treating erectile dysfunction in males and **sexual  
 dysfunction**, such as sexual arousal disorder, in females. The  
 methods involve administering an effective amt. of certain compds. such as

HP-228 (Ac-Nle-Gln-His(D)Phe-Arg-(D)Trp-Gly-NH2).

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI HP-3228 and related peptides to treat **sexual dysfunction**  
 AB Methods for treating erectile dysfunction in males and **sexual dysfunction**, such as sexual arousal disorder, in females. The methods involve administering an effective amt. of certain compds. such as HP-228 (Ac-Nle-Gln-His(D)Phe-Arg-(D)Trp-Gly-NH2).  
 ST peptide HP228 **sexual dysfunction melanocortin** antagonist; erectile dysfunction peptide HP228 **melanocortin** receptor  
 IT Sexual behavior  
 (disorder; HP-3228 and related peptides to treat **sexual dysfunction**)  
 IT Sexual behavior  
 (impotence; HP-3228 and related peptides to treat **sexual dysfunction**)  
 IT Pituitary hormone receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (melanocortin 3; HP-3228 and related peptides to treat **sexual dysfunction**)  
 IT 172617-89-9P, HP-228  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (HP-3228 and related peptides to treat **sexual dysfunction**)  
 IT 7565-89-1 170103-02-3 170103-04-5 182687-57-6 182687-58-7  
 182687-61-2 205499-42-9 205499-43-0 223473-41-4, HP 467  
 252047-01-1 252047-02-2 252047-03-3 252047-04-4 252047-05-5  
 252047-06-6 252047-07-7 252047-08-8 252047-09-9 252047-10-2  
 252047-11-3 252047-12-4 252047-13-5  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (HP-3228 and related peptides to treat **sexual dysfunction**)  
 IT 128908-32-7, **Melanocortin**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (HP-3228 and related peptides to treat **sexual dysfunction**)

L20 ANSWER 12 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 135:175427 CA

TITLE: Uses of agrp-melanocortin receptor binding modulating compounds

INVENTOR(S): Hadcock, John Richard Neville; Swick, Andrew Gordon

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 23 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1125579	A2	20010822	EP 2001-300233	20010111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO

US 2002065277	A1	20020530	US 2001-761320	20010116
BR 2001000106	A	20010828	BR 2001-106	20010118
JP 2001242173	A2	20010907	JP 2001-9643	20010118

PRIORITY APPLN. INFO.:

US 2000-176508P P 20000118

US 2000-206126P P 20000522

AB The present invention provides a method of treating obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the step of administering to a patient having or at risk of having one of the above-mentioned diseases a therapeutically effective amt. of a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not attenuate the binding of .alpha.-MSH to **melanocortin** receptors. The present invention also provides a method of identifying a compd. that is useful for the treatment or prevention of obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the steps of: (1) detg. if a compd. affects the binding of agouti-related protein to **melanocortin** receptors; (2) detg. if a compd. affects the binding of .alpha.-MSH to **melanocortin** receptors; and (3) selecting a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not affect the binding of .alpha.-MSH to **melanocortin** receptors.

TI Uses of agrp-**melanocortin** receptor binding modulating compounds

AB The present invention provides a method of treating obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the step of administering to a patient having or at risk of having one of the above-mentioned diseases a therapeutically effective amt. of a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not attenuate the binding of .alpha.-MSH to **melanocortin** receptors. The present invention also provides a method of identifying a compd. that is useful for the treatment or prevention of obesity, **sexual dysfunction** (including erectile dysfunction), diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal dysfunction, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia, or substance abuse, the method comprising the steps of: (1) detg. if a compd. affects the binding of agouti-related protein to **melanocortin** receptors; (2) detg. if a compd. affects the binding of .alpha.-MSH to **melanocortin** receptors; and (3) selecting a compd. that attenuates the binding of agouti-related protein to **melanocortin** receptors, but does not affect the binding of .alpha.-MSH to **melanocortin** receptors.

ST agouti related protein **melanocortin** receptor binding modulator

IT Drugs of abuse

(abuse of, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

- (agouti-related; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Antiarteriosclerotics  
(antiatherosclerotics; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Sexual behavior  
(disorder, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Lipoproteins  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (hyperlipoproteinemia, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Sexual behavior  
(impotence, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Radiochemical analysis  
(in drug screening; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Pituitary hormone receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(**melanocortin** 3; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Pituitary hormone receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(**melanocortin** 4; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Pituitary hormone receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(**melanocortin**; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Diabetes mellitus  
(non-insulin-dependent, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)
- IT Disease, animal  
(syndrome X, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with



**melanocortin** receptor agonists and other agents)

IT Anticholesteremic agents  
 Antidiabetic agents  
 Antihypertensives  
 Antiobesity agents  
 Drug delivery systems  
 Drug interactions  
 Drug screening  
 (therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT Adrenal gland, disease  
 Alcoholism  
 Hypertriglyceridemia  
 (treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

IT 9004-10-8, Insulin, biological studies  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (hyperinsulinemia and resistance, treatment; therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with other agents)

IT 37213-49-3, .alpha.-MSH  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (therapeutic uses of agouti-related protein (agrp)-**melanocortin** receptor binding modulating compds. that do not affect binding of .alpha.-MSH and combination with **melanocortin** receptor agonists and other agents)

L20 ANSWER 13 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 134:116238 CA

TITLE: **Melanocortin** receptor-3 ligands to treat **sexual dysfunction**

INVENTOR(S): Dines, Kevin C.; Gahman, Timothy C.; Girtten, Beverly E.; Hitchin, Douglas L.; Holme, Kevin R.; Lang, Hengyuan; Slivka, Sandra R.; Watson-Straughan, Karen J.; Tuttle, Ronald R.; Pei, Yazhong

PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005401	A1	20010125	WO 2000-US19408	20000713
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,			

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6284735 B1 20010904 US 1999-356386 19990716  
PRIORITY APPLN. INFO.: US 1999-356386 A2 19990716  
US 1999-364825 A2 19990730  
US 1999-401004 A2 19990921  
US 1998-83368P P 19980428  
US 1999-301391 A1 19990428  
US 1999-306686 A2 19990506

OTHER SOURCE(S): MARPAT 134:116238

AB Methods for treating **sexual dysfunction**, such as  
erectile dysfunction or sexual arousal disorder, with a compd. having the  
generic formula X1-X2-D-Phe-Arg-D-Trp-X3 [X1 = R1R2NCHR3CY1Y2, Ac, H, or  
absent, where R1 = R2, COPh, CO2Bu-t, CO2CH2Ph, CHCO-(polyethylene glycol)  
or A which is N,O-(un)substituted 3-amino-4,5,6-trihydroxytetrahydro-2-  
pyranyl; R2 = H, Ac, Et, PhCH2; R3 = alkyl, cycloalkyl; Y1, Y2 = H or  
together form carbonyl or thiocarbonyl; X2 = NR1CHR4CY1Y2-His, His, Ac, or  
H, where R4 = (CH2)mCONH2, (CH2)mCONHR1, or (CH2)CONHA (m = 1-3); X3 =  
NR1CHR6(CH2)nCY1Y2R5 or R5, where R5 = OH, OR3, NH2, SH, NHMe, NHCH2PH, or  
A; R6 = H or R3, n = 0-3]. A particularly useful compd. is HP-228, which  
has the formula Ac-Nle-Gln-His-D-Phe-Arg-D-Trp-Gly-NH2. The invention  
also provides methods for selecting **melanocortin** receptor-3  
ligands by detg. whether a compd. modulates the activity of MC-3 as an  
agonist or antagonist. These methods can be used to screen compd.  
libraries, including benzimidazoles, for ligands to treat MC-3-assocd.  
conditions. Such conditions include **sexual dysfunction**  
, including erectile dysfunction and sexual arousal disorder (data given).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Melanocortin** receptor-3 ligands to treat **sexual  
dysfunction**

AB Methods for treating **sexual dysfunction**, such as  
erectile dysfunction or sexual arousal disorder, with a compd. having the  
generic formula X1-X2-D-Phe-Arg-D-Trp-X3 [X1 = R1R2NCHR3CY1Y2, Ac, H, or  
absent, where R1 = R2, COPh, CO2Bu-t, CO2CH2Ph, CHCO-(polyethylene glycol)  
or A which is N,O-(un)substituted 3-amino-4,5,6-trihydroxytetrahydro-2-  
pyranyl; R2 = H, Ac, Et, PhCH2; R3 = alkyl, cycloalkyl; Y1, Y2 = H or  
together form carbonyl or thiocarbonyl; X2 = NR1CHR4CY1Y2-His, His, Ac, or  
H, where R4 = (CH2)mCONH2, (CH2)mCONHR1, or (CH2)CONHA (m = 1-3); X3 =  
NR1CHR6(CH2)nCY1Y2R5 or R5, where R5 = OH, OR3, NH2, SH, NHMe, NHCH2PH, or  
A; R6 = H or R3, n = 0-3]. A particularly useful compd. is HP-228, which  
has the formula Ac-Nle-Gln-His-D-Phe-Arg-D-Trp-Gly-NH2. The invention  
also provides methods for selecting **melanocortin** receptor-3  
ligands by detg. whether a compd. modulates the activity of MC-3 as an  
agonist or antagonist. These methods can be used to screen compd.  
libraries, including benzimidazoles, for ligands to treat MC-3-assocd.  
conditions. Such conditions include **sexual dysfunction**  
, including erectile dysfunction and sexual arousal disorder (data given).

ST peptide prepn **melanocortin** receptor **sexual  
dysfunction**; benzimidazole combinatorial library  
**melanocortin** receptor **sexual dysfunction**

IT Sexual behavior  
(disorder; **melanocortin** receptor-3 ligands to treat  
**sexual dysfunction**)

IT Combinatorial library  
(**melanocortin** receptor-3 ligands to treat **sexual  
dysfunction**)

IT Peptides, preparation  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (melanocortin receptor-3 ligands to treat **sexual dysfunction**)

IT Pituitary hormone receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(melanocortin; melanocortin receptor-3 ligands to treat **sexual dysfunction**)

IT 172617-89-9P, Hp-228  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(melanocortin receptor-3 ligands to treat **sexual dysfunction**)

IT 7565-89-1P 170103-02-3P 170103-04-5P 170103-05-6P 182687-55-4P  
 182687-56-5P 182687-57-6P 182687-58-7P 182687-59-8P 182687-60-1P  
 182687-61-2P 205499-42-9P 205499-43-0P 223473-41-4P, HP 467  
 252047-01-1P 252047-02-2P 252047-03-3P 252047-04-4P 252047-05-5P  
 252047-06-6P 252047-09-9P 252047-10-2P 252047-11-3P 252047-12-4P  
 252047-13-5P 321180-15-8P 321180-17-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(melanocortin receptor-3 ligands to treat **sexual dysfunction**)

IT 248947-36-6 321180-43-2 321180-45-4 321180-47-6 321180-49-8  
 321180-51-2 321180-53-4 321180-55-6 321180-57-8 321180-59-0  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(melanocortin receptor-3 ligands to treat **sexual dysfunction**)

L20 ANSWER 14 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 134:76409 CA

TITLE: Compositions and methods for treatment of **sexual dysfunction**

INVENTOR(S): Blood, Christine H.; Shadiack, Annette M.; Bernstein, Joanna K.; Herbert, Guy W.

PATENT ASSIGNEE(S): Palatin Technologies Inc., USA

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000224	A1	20010104	WO 2000-US18217	20000629
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

BR 2000012200 A 20020326 BR 2000-12200 20000629  
 EP 1196184 A1 20020417 EP 2000-950283 20000629  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-142346P P 19990629  
 US 2000-194987P P 20000405  
 US 2000-606501 A 20000628  
 WO 2000-US18217 W 20000629

AB Compns. and methods are provided for the treatment of **sexual dysfunctions** in mammals, such as erectile dysfunction and female **sexual dysfunction**. In one embodiment, a peptide-based compn. including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH is administered. Methods of administration include injection, oral, nasal and mucosal administration.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Compositions and methods for treatment of **sexual dysfunction**

AB Compns. and methods are provided for the treatment of **sexual dysfunctions** in mammals, such as erectile dysfunction and female **sexual dysfunction**. In one embodiment, a peptide-based compn. including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH is administered. Methods of administration include injection, oral, nasal and mucosal administration.

ST **sexual dysfunction melanocortin analog**  
 peptide

IT Drug delivery systems  
 (buccal; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Sexual behavior  
 (disorder, female; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Sexual behavior  
 (impotence; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems  
 (inhalants; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems  
 (injections; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Pituitary hormone receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (**melanocortin**; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems  
 (mucosal; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems  
 (nasal; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems  
 (oral; **melanocortin** analogs for treating **sexual dysfunctions**)

IT Drug delivery systems  
 (topical; **melanocortin** analogs for treating **sexual dysfunctions**)

IT 4289-02-5 31008-44-3 189691-06-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**melanocortin** analogs for treating **sexual dysfunctions**)

L20 ANSWER 15 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 134:42445 CA

TITLE: Preparation of piperidine amino acid derivatives as **melanocortin-4** receptor agonists

INVENTOR(S): Bakshi, Raman K.; Barakat, Khaled J.; Nargund, Ravi P.; Palucki, Brenda L.; Patchett, Arthur A.; Sebhat, Iyassu; Ye, Zhixiong; Van, Der Ploeg Leonardus H. T.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Van Der Ploeg, Leonardus H. T.

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074679	A1	20001214	WO 2000-US14930	20000531
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1187614	A1	20020320	EP 2000-937961	20000531
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
US 6350760	B1	20020226	US 2000-585111	20000601
PRIORITY APPLN. INFO.:			US 1999-137477P	P 19990604
			US 1999-169209P	P 19991202
			WO 2000-US14930	W 20000531

OTHER SOURCE(S): MARPAT 134:42445

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Piperidine derivs. I [R2C2 = aryl, 5- or 6-membered heteroaryl or heterocyclyl, 5- to 7-membered carbocyclyl, which may be substituted; L = (CRb2)m, where Rb = H, alkyl, (CH2)n-cycloalkyl or -aryl; m = 0-2, n = 0-3; X, Y = (CH2)0-2; Ra = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -O(CH2)n-aryl, which may be substituted; Re = H, alkyl, (CH2)n-aryl, -cycloalkyl, -heteroaryl, which may be substituted, acyl, sulfonyl, etc.; R1 = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -heterocyclyl; R2 = any group given for R1, CN, (CH2)n-carboxamido, -carboxy, -acylamino, sulfonylamino, -amino, etc.] were prepd. as agonists of the human **melanocortin** receptors, in particular, the human **melanocortin-4** receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual**

**dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Thus, II trifluoroacetate, prepd. by coupling of Et 1-(D-4-chlorophenylalanyl)-4-cyclohexyl-4-[(1,2,4-triazol-1-yl)methyl]piperidine trifluoroacetate (prepn. given) with N-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Boc-D-Tic), was > 2,200-fold, > 10,000-fold, and > 580-fold selective for the human MC-4R over human MC-1R, MC-2R, and MC-3R, resp.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

- TI Preparation of piperidine amino acid derivatives as **melanocortin**-4 receptor agonists
- AB Piperidine derivs. I [R2C2 = aryl, 5- or 6-membered heteroaryl or heterocyclyl, 5- to 7-membered carbocyclyl, which may be substituted; L = (CRb2)m, where Rb = H, alkyl, (CH2)n-cycloalkyl or -aryl; m = 0-2, n = 0-3; X, Y = (CH2)0-2; Ra = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -O(CH2)n-aryl, which may be substituted; Re = H, alkyl, (CH2)n-aryl, -cycloalkyl, -heteroaryl, which may be substituted, acyl, sulfonyl, etc.; R1 = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -heterocyclyl; R2 = any group given for R1, CN, (CH2)n-carboxamido, -carboxy, -acylamino, sulfonylamino, -amino, etc.] were prepd. as agonists of the human **melanocortin** receptors, in particular, the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, **sexual dysfunction**, including erectile dysfunction and female **sexual dysfunction**. Thus, II trifluoroacetate, prepd. by coupling of Et 1-(D-4-chlorophenylalanyl)-4-cyclohexyl-4-[(1,2,4-triazol-1-yl)methyl]piperidine trifluoroacetate (prepn. given) with N-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Boc-D-Tic), was > 2,200-fold, > 10,000-fold, and > 580-fold selective for the human MC-4R over human MC-1R, MC-2R, and MC-3R, resp.
- ST piperidine amino acid prepn **melanocortin** receptor agonist
- IT Sexual behavior  
(disorder; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)
- IT Sexual behavior  
(impotence; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)
- IT Pituitary hormone receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(**melanocortin** 4; prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)
- IT Antidiabetic agents  
Antiobesity agents  
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)
- IT Peptides, preparation  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)
- IT Dopamine receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(prepn. of piperidine amino acid derivs. as **melanocortin**-4 receptor agonists)
- IT Adrenoceptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)  
 (.alpha.2; prepn. of piperidine amino acid derivs. as  
**melanocortin-4** receptor agonists)

IT Adrenoceptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (.beta.3; prepn. of piperidine amino acid derivs. as  
**melanocortin-4** receptor agonists)

IT 312637-61-9P 312637-63-1P 312637-77-7P 312637-91-5P 312638-30-5P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT  
 (Reactant or reagent); USES (Uses)  
 (prepn. of piperidine amino acid derivs. as **melanocortin-4**  
 receptor agonists)

IT 312637-47-1P 312637-48-2P 312637-49-3P 312637-51-7P 312637-53-9P  
 312637-55-1P 312637-57-3P 312637-59-5P 312637-64-2P 312637-65-3P  
 312637-66-4P 312637-67-5P 312637-68-6P 312637-70-0P 312637-72-2P  
 312637-73-3P 312637-75-5P 312637-79-9P 312637-81-3P 312637-82-4P  
 312637-83-5P 312637-85-7P 312637-87-9P 312637-89-1P 312637-90-4P  
 312637-92-6P 312637-93-7P 312637-94-8P 312637-95-9P 312637-96-0P  
 312637-97-1P 312637-98-2P 312637-99-3P 312638-00-9P 312638-02-1P  
 312638-04-3P 312638-06-5P 312638-08-7P 312638-10-1P 312638-11-2P  
 312638-13-4P 312638-15-6P 312638-17-8P 312638-19-0P 312638-21-4P  
 312638-23-6P 312638-24-7P 312638-26-9P 312638-28-1P 312638-29-2P  
 312638-32-7P 312638-33-8P 312638-35-0P 312638-36-1P 312638-37-2P  
 312638-38-3P 312638-40-7P 312638-42-9P 312638-44-1P 312638-46-3P  
 312638-47-4P 312638-48-5P 312638-49-6P 312638-50-9P 312638-52-1P  
 312638-54-3P 312638-56-5P 312638-58-7P 312638-59-8P 312638-60-1P  
 312638-61-2P 312638-62-3P 312638-63-4P 312638-64-5P 312638-65-6P  
 312638-66-7P 312638-67-8P 312638-69-0P 312638-70-3P 312638-71-4P  
 312638-72-5P 312638-73-6P 312638-74-7P 312638-75-8P 312638-77-0P  
 312638-79-2P 312638-81-6P 312639-64-8P 312639-65-9P 312639-66-0P  
 312639-67-1P 312639-68-2P 312639-69-3P 312639-70-6P 312639-71-7P  
 312639-72-8P 312639-73-9P 312639-75-1P 312639-76-2P 312639-77-3P  
 312639-78-4P 312639-80-8P 312639-82-0P 312639-83-1P 312639-84-2P  
 312639-85-3P 312639-87-5P 312639-88-6P 312639-89-7P 312639-90-0P  
 312639-91-1P 312639-92-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of piperidine amino acid derivs. as **melanocortin-4**  
 receptor agonists)

IT 57-88-5, Cholesterol, biological studies 9001-42-7, .alpha.-Glucosidase  
 9028-35-7, HMG-CoA reductase 82785-45-3, Neuropeptide y  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (prepn. of piperidine amino acid derivs. as **melanocortin-4**  
 receptor agonists)

IT 312639-52-4P 312639-53-5P  
 RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic  
 preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of piperidine amino acid derivs. as **melanocortin-4**  
 receptor agonists)

IT 542-69-8, Butyl iodide 24465-45-0 29364-29-2, Sodium  
 2-methyl-2-propanethiolate 29943-42-8, Tetrahydro-4H-pyran-4-one  
 31637-11-3 41253-21-8, 1,2,4-Triazole sodium salt 57292-44-1  
 115962-35-1 136465-81-1 142851-03-4 150417-15-5 167262-68-2  
 207342-56-1 273378-16-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of piperidine amino acid derivs. as **melanocortin-4**  
receptor agonists)

IT 10462-00-7P 115238-58-9P 142001-86-3P 158144-85-5P 188916-68-9P  
225240-55-1P 252008-88-1P 312638-82-7P 312638-83-8P 312638-84-9P  
312638-86-1P 312638-87-2P 312638-88-3P 312638-89-4P 312638-91-8P  
312638-93-0P 312638-94-1P 312638-95-2P 312638-96-3P 312638-97-4P  
312638-98-5P 312638-99-6P 312639-00-2P 312639-01-3P 312639-02-4P  
312639-03-5P 312639-04-6P 312639-06-8P 312639-08-0P 312639-09-1P  
312639-11-5P 312639-12-6P 312639-13-7P 312639-14-8P 312639-15-9P  
312639-16-0P 312639-17-1P 312639-18-2P 312639-19-3P 312639-20-6P  
312639-21-7P 312639-22-8P 312639-23-9P 312639-24-0P 312639-25-1P  
312639-26-2P 312639-27-3P 312639-28-4P 312639-29-5P 312639-30-8P  
312639-31-9P 312639-32-0P 312639-33-1P 312639-34-2P 312639-35-3P  
312639-36-4P 312639-37-5P 312639-38-6P 312639-39-7P 312639-40-0P  
312639-41-1P 312639-42-2P 312639-43-3P 312639-44-4P 312639-45-5P  
312639-46-6P 312639-47-7P 312639-48-8P 312639-49-9P 312639-50-2P  
312639-51-3P 312639-54-6P 312639-55-7P 312639-56-8P 312639-57-9P  
312639-58-0P 312639-59-1P 312639-60-4P 312639-61-5P 312639-62-6P  
312639-63-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(prepn. of piperidine amino acid derivs. as **melanocortin-4**  
receptor agonists)

IT 9004-10-8D, Insulin, mimetic, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of piperidine amino acid derivs. as **melanocortin-4**  
receptor agonists)

IT 9025-82-5, Phosphodiesterase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)

(type V cyclic-GMP-selective phosphodiesterase inhibitor; prepn. of  
piperidine amino acid derivs. as **melanocortin-4** receptor  
agonists)

L20 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 132:22957 CA

TITLE: Preparation of spiro piperidine derivatives as  
**melanocortin** receptor agonists

INVENTOR(S): Nargund, Ravi P.; Ye, Zhixiong; Palucki, Brenda L.;  
Bakshi, Raman K.; Patchett, Arthur A.; Van Der Ploeg,  
Leonardus H. T.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 77 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964002	A1	19991216	WO 1999-US13252	19990610
W:				
AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD,				
GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV,				
MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR,				
TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946801	A1	19991230	AU 1999-46801	19990610

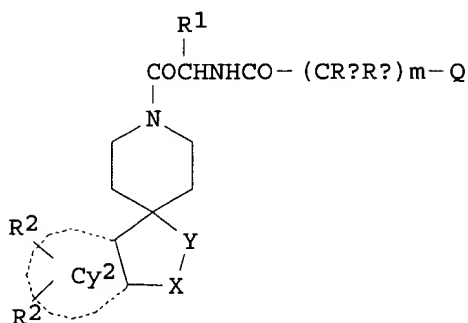


AU 742425 B2 20020103  
 EP 1085869 A1 20010328 EP 1999-930220 19990610  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,  
 SI, LT, LV, FI, RO  
 US 6294534 B1 20010925 US 1999-329814 19990610  
 JP 2002517444 T2 20020618 JP 2000-553071 19990610  
 US 2001029259 A1 20011011 US 2001-781373 20010212  
 US 6410548 B2 20020625

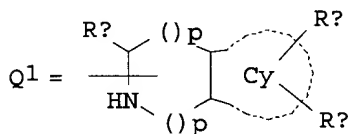
PRIORITY APPLN. INFO.:

US 1998-88908P P 19980611  
 GB 1998-17179 A 19980806  
 US 1999-123260P P 19990308  
 US 1999-329814 A3 19990610  
 WO 1999-US13252 W 19990610

OTHER SOURCE(S): MARPAT 132:22957  
 GI



I



AB Certain novel spiroperidine compds. I [Cy2 = six-membered arom. ring contg. 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclyl, 5 or 6 membered carbocyclyl; m, p, q independently = 0, 1, or 2] are agonists of **melanocortin** receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of **melanocortin** receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of spiroperidine derivatives as **melanocortin**

receptor agonists

AB Certain novel spiroperidone compds. I [Cy2 = six-membered arom. ring contg. 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclyl, 5 or 6 membered carbocyclyl; m, p, q independently = 0, 1, or 2] are agonists of **melanocortin** receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of **melanocortin** receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, **sexual dysfunction** including erectile dysfunction and female **sexual dysfunction**.

ST spiroperidone prepn **melanocortin** receptor agonist; obesity treatment spiroperidone; diabetes treatment spiroperidone; **sex dysfunction** treatment spiroperidone

IT Pituitary hormone receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**melanocortin**; prepn. of and effect of spiroperidone derivs.)

IT	252008-17-6P	252008-18-7P	252008-19-8P	252008-20-1P	252008-21-2P
	252008-23-4P	252008-24-5P	252008-25-6P	252008-26-7P	252008-27-8P
	252008-28-9P	252008-29-0P	252008-31-4P	252008-33-6P	252008-35-8P
	252008-37-0P	252008-38-1P	252008-39-2P	252008-40-5P	252008-41-6P
	252008-42-7P	252008-43-8P	252008-44-9P	252008-45-0P	252008-46-1P
	252008-47-2P	252008-48-3P	252008-49-4P	252008-50-7P	252008-51-8P
	252008-52-9P	252008-53-0P	252008-54-1P	252008-55-2P	252008-56-3P
	252008-57-4P	252008-58-5P	252008-60-9P	252008-61-0P	252008-62-1P
	252008-63-2P	252008-64-3P	252008-65-4P	252008-66-5P	252008-67-6P
	252008-68-7P	252008-69-8P			

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiroperidone derivs. as **melanocortin** receptor agonists)

IT	109-02-4, N-Methylmorpholine	2592-95-2, 1-Hydroxybenzotriazole
	2627-86-3	3886-69-9
	24424-99-5, Di-tert-butyl dicarbonate	
	40949-94-8, Potassium bis(trimethylsilyl)amide	57292-44-1
	70601-64-8	
	78879-20-6	101752-05-0
	115962-35-1	132705-51-2
	134166-72-6,	
	D-4-Chlorophenylalanine methyl ester	136465-81-1
	137419-24-0	
	142335-42-0	159634-86-3
	252008-90-5	

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of spiroperidone derivs. as **melanocortin** receptor agonists)

IT	115238-59-0P	159634-59-0P	185526-14-1P	185526-28-7P	185526-32-3P
	185526-40-3P	185526-41-4P	252008-70-1P	252008-71-2P	252008-72-3P
	252008-73-4P	252008-74-5P	252008-75-6P	252008-76-7P	252008-77-8P
	252008-78-9P	252008-79-0P	252008-80-3P	252008-81-4P	252008-82-5P
	252008-83-6P	252008-84-7P	252008-85-8P	252008-86-9P	252008-87-0P
	252008-89-2P	252008-91-6P	252008-92-7P	252008-93-8P	252008-94-9P
	252008-95-0P	252008-96-1P	252008-97-2P	252008-98-3P	252008-99-4P
	252009-00-0P	252009-01-1P	252009-02-2P	252009-03-3P	252009-04-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of spiroperidone derivs. as **melanocortin** receptor agonists)

=> d his

09/990,499

(FILE 'HOME' ENTERED AT 10:41:47 ON 06 AUG 2002)

FILE 'CA' ENTERED AT 10:41:55 ON 06 AUG 2002

L1 12 S MC-4R  
L2 1327 S BIND (2A) SELECT?  
L3 80191 S AGONIST  
L4 6637 S MED OR (MALE ERECT? DYSFUN?)  
L5 1 S L4 AND L2  
L6 53 S L4 AND L3  
L7 54 S L5 OR L6  
L8 41 S L7 NOT PY>1999  
L9 76 S MALE ERECT? DYSFUN?  
L10 531 S SEX? DYSFUN?  
L11 590 S L9 OR L10  
L12 932 S MELANOCORTIN  
L13 16 S L11 AND L12  
L14 0 S L13 NOT PY>1999  
L15 27472 S MC  
L16 167019 S ME (2A) R  
L17 266 S MC (2A) R  
L18 148 S MC (2W) R  
L19 1065 S L18 OR L12  
L20 16 S L19 AND L11

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 10:50:17 ON 06 AUG 2002